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=> d his

     (FILE 'HOME' ENTERED AT 16:22:45 ON 25 SEP 2003)

     FILE 'BIOSIS' ENTERED AT 16:23:56 ON 25 SEP 2003
L1           968 S PRICE P?/AU
L2          1495 S FETUIN
L3             5 S L1 AND L2
L4        390653 S CALCIUM
L5            65 S L4 AND L2
L6            60 S L5 NOT L3

     FILE 'WPIDS' ENTERED AT 16:40:53 ON 25 SEP 2003
L7             4 S L5

     FILE 'USPATFULL' ENTERED AT 16:42:58 ON 25 SEP 2003
L8           498 S FETUIN
L9        270777 S CALCIUM
L10           15 S L8 (P) L9

=> log hold
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 4.30      70.32

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 16:44:19 ON 25 SEP 2003
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=> d his

     (FILE 'HOME' ENTERED AT 09:52:28 ON 26 SEP 2003)

     FILE 'MEDLINE' ENTERED AT 09:52:33 ON 26 SEP 2003
L1          1084 S FETUIN
L2         64652 S ARTERIOSCLEROSIS
L3             3 S L1 AND L2

=> log hold
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.91       3.12

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 09:56:22 ON 26 SEP 2003
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substance identification.

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=> s fetuin and arteriosclerosis
          490 FETUIN
         7462 ARTERIOSCLEROSIS
L1          32 FETUIN AND ARTERIOSCLEROSIS

=> d l1 1-32

L1   ANSWER 1 OF 32  USPATFULL on STN
AN     2003:245126  USPATFULL
TI     Novel protein zlmda33
IN     Conklin, Darrell C., Seattle, WA, UNITED STATES
       Gao, Zeren, Redmond, WA, UNITED STATES
PI     US 2003171540      A1   20030911
AI     US 2001-12143      A1   20011108 (10)
PRAI   US 2000-247538P     20001109 (60)
DT     Utility
FS     APPLICATION
LN.CNT 2465
INCL   INCLM: 530/350.000
       INCLS: 536/023.500; 435/069.100; 435/325.000; 435/320.100
NCL    NCLM:  530/350.000
       NCLS:  536/023.500; 435/069.100; 435/325.000; 435/320.100
IC     [7]
       ICM: C07K014-435
       ICS: C07H021-04; C12P021-02; C12N005-06

L1   ANSWER 2 OF 32  USPATFULL on STN
AN     2003:206834  USPATFULL
TI     Chemokine beta-1 fusion proteins
IN     Bell, Adam, Germantown, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
PI     US 2003143191      A1   20030731
AI     US 2002-153604     A1   20020524 (10)
PRAI   US 2001-293212P     20010525 (60)
DT     Utility
FS     APPLICATION
LN.CNT 15446
INCL   INCLM: 424/085.100
       INCLS: 530/351.000; 536/023.500; 435/069.500; 435/320.100; 435/325.000
NCL    NCLM:  424/085.100
       NCLS:  530/351.000; 536/023.500; 435/069.500; 435/320.100; 435/325.000
IC     [7]
       ICM: A61K038-19
       ICS: C07K014-52; C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1   ANSWER 3 OF 32  USPATFULL on STN
AN     2003:152750  USPATFULL
TI     Cytokine protein family
IN     Sheppard, Paul O., Granite Falls, WA, UNITED STATES
       Fox, Brian A., Seattle, WA, UNITED STATES
       Klucher, Kevin M., Bellevue, WA, UNITED STATES
       Taft, David W., Kirkland, WA, UNITED STATES
       Kindsvogel, Wayne, Seattle, WA, UNITED STATES
PI     US 2003104416      A1   20030605
AI     US 2002-127816     A1   20020419 (10)
PRAI   US 2001-285408P     20010420 (60)
       US 2001-286482P     20010425 (60)
       US 2001-341050P     20011022 (60)
       US 2001-341105P     20011022 (60)
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L3 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:432214 BIOSIS
DN PREV200300432214
TI Bone origin of the serum complex of calcium, phosphate, **fetuin**, and matrix Gla protein: Biochemical evidence for the cancellous bone remodeling compartment.
AU **Price, P. A. (1)**; Caputo, J. M. (1); Williamson, M. K. (1)
CS (1) Division of Biology, University of California, San Diego, La Jolla, CA, USA USA
SO Journal of Bone and Mineral Research, (September 2002, 2002) Vol. 17, No. Suppl 1, pp. S400. print.
Meeting Info.: Twenty-Fourth Annual Meeting of the American Society for Bone and Mineral Research San Antonio, Texas, USA September 20-24, 2002 American Society for Bone and Mineral Research
. ISSN: 0884-0431.
DT Conference
LA English

L3 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:363448 BIOSIS
DN PREV200300363448
TI Biochemical characterization of the serum **fetuin**-mineral complex.
AU **Price, Paul A. (1)**; Nguyen, Thao Minh Thi; Williamson, Matthew K.
CS (1) Div. of Biology, University of California, San Diego, 0368, La Jolla, CA, 92093-0368, USA: pprice@ucsd.edu USA
SO Journal of Biological Chemistry, (June 13 2003) Vol. 278, No. 24, pp. 22153-22160. print.
ISSN: 0021-9258.
DT Article
LA English
AB The present study was carried out to characterize the **fetuin**-mineral complex (FMC), a high molecular mass complex of calcium phosphate mineral and the proteins **fetuin** and matrix Gla protein (MGP) that was initially discovered in serum of rats treated with etidronate and appears to play a critical role in inhibiting calcification in vivo. **Fetuin** purified from the FMC contains 3.3 mol of protein-bound phosphate. There is 1.3 mg of FMC/ml of serum 6h after etidronate injection, and the FMC is 46% **fetuin** and 53% mineral by mass. Formation of the FMC in the first 6 h after etidronate injection does not increase serum **fetuin** despite the fact that 50% of serum **fetuin** is associated with the FMC, and clearance of the FMC in the 9-24-h interval lowers total serum **fetuin** by 50%. These observations suggest that the **fetuin** component of the FMC is derived from **fetuin** initially in serum and that clearance of the FMC removes the associated **fetuin** from circulation. One additional protein was consistently present in all preparations of the FMC, spp24 (secreted phosphoprotein 24). This 24-kDa protein is similar in domain structure to **fetuin** and, like **fetuin** and MGP, contains several residues of phosphoserine and accumulates in bone. Exogenous spp24 associated strongly with the FMC when added to serum containing it. These observations suggest that spp24 may, like **fetuin** and MGP, play a role in inhibiting calcification.

L3 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:363447 BIOSIS
DN PREV200300363447
TI The inhibition of calcium phosphate precipitation by **fetuin** is accompanied by the formation of a **fetuin**-mineral complex.
AU **Price, Paul A. (1)**; Lim, Joo Eun
CS (1) Div. of Biology, University of California, San Diego, 0368, La Jolla, CA, 92093-0368, USA: pprice@ucsd.edu USA

SO Journal of Biological Chemistry, (June 13 2003) Vol. 278, No. 24, pp. 22144-22152. print.
ISSN: 0021-9258.
DT Article
LA English
AB The present studies show that the previously reported ability of **fetuin** to inhibit the precipitation of hydroxy-apatite from supersaturated solutions of calcium and phosphate in vitro is accompanied by the formation of the **fetuin**-mineral complex, a high molecular mass complex of calcium phosphate mineral and the proteins **fetuin** and matrix Gla protein that was initially discovered in the serum of rats treated with etidronate and that appears to play a critical role in inhibiting calcification in vivo. Rat serum potently inhibited the precipitation of calcium phosphate mineral when the concentration of calcium and phosphate were increased by 10 mM each, and the modified serum was incubated at 37 degreeC for 9 days; in the absence of serum, precipitation occurred in seconds. Large amounts of the **fetuin** -mineral complex were generated in the first 3 h of this incubation and remained throughout the 9-day incubation. Purified bovine **fetuin** inhibited the precipitation of mineral for over 14 days in a solution containing 5 mM calcium and phosphate at pH 7.4 at 22 degreeC, whereas precipitation occurred in minutes without **fetuin**. There was a biphasic drop in ionic calcium in the **fetuin** solution, however, from 5 to 3 mM in the first hour and from 3 to 0.9 mM between 20 and 24 h; these changes in ionic calcium are due to the formation of complexes of calcium, phosphate, and **fetuin**. The complex found at 24 h to 14 days is identical to the **fetuin**-mineral complex found in the serum of etidronate-treated rats, whereas the complex found between 1 and 20 h is less stable.

L3 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:7714 BIOSIS
DN PREV200300007714
TI Bone origin of the serum complex of calcium, phosphate, **fetuin**, and matrix Gla protein: Biochemical evidence for the cancellous bone-remodeling compartment.
NPA
AU **Price, Paul A. (1)**; Caputo, Jeffrey M.; Williamson, Matthew K.
CS (1) Division of Biology, University of California, San Diego, 0368, La Jolla, CA, 92093-0368, USA USA
SO Journal of Bone and Mineral Research, (July 2002, 2002) Vol. 17, No. 7, pp. 1171-1179. print.
ISSN: 0884-0431.
DT Article
LA English
AB We previously described the discovery of a **fetuin**-matrix Gla protein (MGP)-mineral complex in the serum of rats treated with the bone-active bisphosphonate etidronate and showed that the appearance of this complex in serum correlates with the inhibition of bone mineralization by etidronate. In this study we show that the inhibition of bone resorption by treatment with the hormone calcitonin, the cytokine osteoprotegerin, or the drug alendronate, completely inhibits the generation of the **fetuin**-mineral complex in response to etidronate injection. These observations can be explained best by the bone-remodeling compartment (BRC), a cancellous bone compartment in which the concentrations of calcium and phosphate are determined directly by the combined actions of the osteoclast and the osteoblast. When bone mineralization is acutely inhibited by etidronate, the BRC model predicts that the continuing action of osteoclasts will cause a sharp rise in the concentrations of calcium and phosphate in the aqueous solution of the BRC with the consequent spontaneous formation of calcium phosphate crystal nuclei in which growth then would be arrested by formation of a complex with **fetuin**. When the inhibition of bone resorption by calcitonin, osteoprotegerin, or alendronate is combined with the acute inhibition of bone mineralization with etidronate, the BRC model correctly

predicts that there will no longer be a sharp rise in calcium and phosphate, and, therefore, there will no longer be the formation of the **fetuin**-mineral complex. The vascular nature of the BRC is supported by the observations that the **fetuin** component of the **fetuin**-mineral complex is derived from plasma **fetuin** and that the **fetuin** mineral complex appears in plasma within minutes of the inhibition of bone mineralization with etidronate.

L3 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:185181 BIOSIS
DN PREV200200185181
TI Discovery of a high molecular weight complex of calcium, phosphate, **fetuin**, and matrix gamma-carboxyglutamic acid protein in the serum of etidronate-treated rats.
AU **Price, Paul A. (1)**; Thomas, Gethin R.; Pardini, Aaron W.; Figueira, William F.; Caputo, Jeffrey M.; Williamson, Matthew K.
CS (1) Div. of Biology, University of California, San Diego, 0368, La Jolla, CA, 92093-0368: pprice@ucsd.edu USA
SO Journal of Biological Chemistry, (February 8, 2002) Vol. 277, No. 6, pp. 3926-3934. http://www.jbc.org/. print.
ISSN: 0021-9258.
DT Article
LA English
AB In the present study we report the discovery of a novel protein-mineral complex in the serum of rats treated with doses of the bone-active bisphosphonate etidronate that inhibit normal bone mineralization. The composition of this high molecular mass protein-mineral complex consists of about 18% mineral, 80% **fetuin**, and 2% matrix Gla protein (MGP) by weight, and the presence of the complex in serum after an injection of 8 mg etidronate/100 g of body weight elevates calcium by 1.8-fold (to 4.3 mM), phosphate by 1.6-fold (to 5.6 mM), and MGP by 25-fold (to 12 mug/ml). The serum mineral complex reaches maximal levels at 6 h after subcutaneous injection of etidronate and is subsequently cleared from serum by 24 h. This highly specific complex of **fetuin**, MGP, and mineral prevents the growth, aggregation, and precipitation of the mineral component, which indicates that the previously reported calcification inhibitory activities of **fetuin** and MGP may be related to their ability to form stable complexes with nascent mineral nuclei. Treatment with the vitamin K-antagonist warfarin prevents the increase in serum MGP after etidronate injection, which shows that the increase in serum MGP is due to new synthesis and that the gamma-carboxylation of MGP is necessary for its binding to the serum mineral complex.

=>

ANSWER 15 OF 60 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 2001:275500 BIOSIS

DN PREV200100275500

TI Systemic inhibition of spontaneous calcification by the serum protein alpha2-HS glycoprotein/**fetuin**.

AU Jahnen-Dechent, W. (1); Schaefer, C.; Heiss, A.; Groetzinger, J.

CS (1) IZKF BIOMAT Klinikum der RWTH Aachen, Pauwelsstr. 30, 52074, Aachen: willi.jahnen@rwth-aachen.de Germany

SO Zeitschrift fuer Kardiologie, (2001) Vol. 90, No. Supplement 3, pp. III/47-III/56. print.
ISSN: 0300-5860.

DT General Review

LA English

SL English

AB The extracellular fluid is a metastable system with regard to **calcium** and phosphate ions. Active inhibitors of calcification must be present in serum to prevent the spontaneous formation of Ca2+cntdotPi solid phases which could otherwise precipitate to cause renal calcinosis and block small blood vessels. alpha2-HS glycoproteins/**fetuins**, AHSGs, are ideal candidates for this function. AHSGs are ubiquitous and highly abundant in serum; they bind **calcium** and efficiently prevent de novo formation of apatitic mineral. Normocalcemic AHSG-deficient mice develop sporadic perivascular calcification. Hypercalcemia induced by dietary means or by hormone treatment results in lethal calcinosis in Ahsg-/- mice. A mineral binding structure is proposed for domain D1 of AHSG suggesting that the proposed EF-hand motif for **calcium** binding does not exist in AHSG. Unlike serum albumin, AHSG does not preferentially bind ionic Ca2+, but rather in the form of apatitic micro-crystals.

L7 ANSWER 2 OF 4 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-475941 [51] WPIDS
DNC C2001-142750
TI Method of inhibiting calcification of a soft tissue for e.g. artery in a mammal involves inhibiting osteoclastic bone resorption in the mammal by administration of a bisphosphonate in a concentration to inhibit bone resorption.
DC B05
IN PRICE, P A
PA (REGC) UNIV CALIFORNIA
CYC 94
PI WO 2001049295 A1 20010712 (200151)* EN 65p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001027567 A 20010716 (200169)
EP 1267888 A1 20030102 (200310) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003519183 W 20030617 (200349) 76p
ADT WO 2001049295 A1 WO 2001-US149 20010102; AU 2001027567 A AU 2001-27567 20010102; EP 1267888 A1 EP 2001-901691 20010102, WO 2001-US149 20010102; JP 2003519183 W JP 2001-549663 20010102, WO 2001-US149 20010102
FDT AU 2001027567 A Based on WO 2001049295; EP 1267888 A1 Based on WO 2001049295; JP 2003519183 W Based on WO 2001049295
PRAI US 2000-477505 20000104
AB WO 200149295 A UPAB: 20010910
NOVELTY - Method of inhibiting calcification of a soft tissue in a mammal involves inhibiting osteoclastic bone resorption by administration of a bisphosphonate in a concentration to inhibit bone resorption.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(a) mitigating the calcification of an implanted prosthetic device in a mammal by administering a low dosage of the bisphosphonate to inhibit calcification of the prosthetic device or soft tissue surrounding the device;

(b) mitigating a symptom of or progression of atherosclerosis in a mammal involving inhibiting the removal of mineral by macrophages at sites of calcification by administering the bisphosphonate in the mammal at a concentration that does not inhibit macrophages at location other than sites of calcification;

(c) a kit for the mitigation of a pathology associated with calcification of the soft tissue comprising a container containing the bisphosphonate and instructional materials teaching the use of the bisphosphonate;

(d) delivering a calcification initiator to a pre-selected site involving providing a **fetuin**-mineral complex attached to a targeting molecule specifically binding to the site and contacting the complex to the site;

(e) a method of distributing mineral nuclei within a matrix involving impregnating the matrix with the complex and denaturing the **fetuin** such that the mineral is released from the complex;

(f) stabilizing a size or crystal structure of a mineral salt (preferably **calcium** or its salt) in an aqueous phase by contacting the mineral salt with the isolated **fetuin**; and

(g) a mineral or mineral salt in an aqueous phase by contacting the mineral salt with the isolated **fetuin**.

ACTIVITY - Osteopathic.

MECHANISM OF ACTION - None given.

USE - For inhibiting calcification of a soft tissue such as an

artery, a heart valve, an atherosclerotic plaque, a cancer, a kidney, a prostate, skin, muscle, cartilage, viscera, and heart muscle in a mammal diagnosed as having or at risk for a pathology characterized by calcification of a soft tissue (preferably a human, a non-human primate, a canine, a feline, an equine, a bovine, a rodent, a porcine and a lagomorph); for mitigating the symptoms of disease such as atherosclerosis, arteriosclerosis, arteriolosclerosis, hypertensive arteriolosclerosis, Monckeberg's arteriosclerosis, heart valve stenosis, uremia, diabetes, hyperparathyroidism, blood clot formation, cancer growth, cancer metastasis, hypertension, vitamin D toxicity and arthritis (all claimed).

ADVANTAGE - The bisphosphonates are able to inhibit bone resorption at far lower dosages than the dosages at which they have been observed to inhibit bone calcification without adversely affecting bone mineralization.

Dwg.0/8

=>

L10 ANSWER 5 OF 15 USPATFULL on STN
AN 2003:37566 USPATFULL
TI Fetuin-MGP-mineral complex in serum
IN Price, Paul A., La Jolla, CA, UNITED STATES
PA The Regents of the University of California (U.S. corporation)
PI US 2003027211 A1 20030206
AI US 2001-45596 A1 20011018 (10)
RLI Continuation-in-part of Ser. No. US 2000-477505, filed on 4 Jan 2000, ABANDONED
DT Utility
FS APPLICATION
LREP QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C., P O BOX 458, ALAMEDA, CA, 94501
CLMN Number of Claims: 75
ECL Exemplary Claim: 1
DRWN 20 Drawing Page(s)
LN.CNT 3126
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods of inhibiting calcification of a soft tissue (e.g., an artery, a heart valve, an atherosclerotic plaque, a cancer, a kidney, a prostate, skin, muscle, cartilage, viscera, and heart muscle) in a mammal. These methods involve inhibiting osteoclastic bone resorption in said mammal (e.g., a mammal diagnosed as having or at risk for a pathology characterized by calcification of a soft tissue). The inhibition is preferably by administration of a bisphosphonate to the mammal in a concentration sufficient to inhibit bone resorption without inhibiting bone mineralization. The methods of this invention can also be used to mitigate a symptom of atherosclerosis in a mammal. Such methods involve inhibiting osteoclastic bone resorption in the mammal. In preferred embodiment, the inhibiting is by administration of a bisphosphonate to the mammal in a concentration sufficient to inhibit bone resorption without inhibiting bone mineralization

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NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
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NEWS 8	Mar 24	PATDPAFULL now available on STN
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NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
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NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation

NEWS 38 AUG 18 Simultaneous left and right truncation added to ANABSTR

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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FILE 'HOME' ENTERED AT 14:36:39 ON 15 SEP 2003

=> file uspatfull
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'USPATFULL' ENTERED AT 14:36:51 ON 15 SEP 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 11 Sep 2003 (20030911/PD)
FILE LAST UPDATED: 11 Sep 2003 (20030911/ED)
HIGHEST GRANTED PATENT NUMBER: US6618858
HIGHEST APPLICATION PUBLICATION NUMBER: US2003172428
CA INDEXING IS CURRENT THROUGH 11 Sep 2003 (20030911/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 11 Sep 2003 (20030911/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2003

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>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate

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       US 2001-285424P     20010420 (60)
DT     Utility
FS     APPLICATION
LN.CNT 6151
INCL   INCLM: 435/006.000
NCL    NCLM:  435/006.000
IC     [7]
       ICM: C12Q001-68
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1   ANSWER 4 OF 32  USPATFULL on STN
AN     2003:145864  USPATFULL
TI     Human cytokine receptor
IN     Presnell, Scott R., Tacoma, WA, UNITED STATES
       Xu, Wenfeng, Mukilteo, WA, UNITED STATES
       Kindsvogel, Wayne, Seattle, WA, UNITED STATES
       Chen, Zhi, Bellevue, WA, UNITED STATES
       Hughes, Steven D., Seattle, WA, UNITED STATES
PI     US 2003099608      A1   20030529
AI     US 2002-104919     A1   20020322 (10)
PRAI   US 2001-279222P     20010327 (60)
DT     Utility
FS     APPLICATION
LN.CNT 9645
INCL   INCLM: 424/085.100
       INCLS: 435/069.500; 435/320.100; 435/325.000; 530/351.000; 536/023.500
NCL    NCLM:  424/085.100
       NCLS:  435/069.500; 435/320.100; 435/325.000; 530/351.000; 536/023.500
IC     [7]
       ICM: A61K038-19
       ICS: C07K014-52; C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1   ANSWER 5 OF 32  USPATFULL on STN
AN     2003:140498  USPATFULL
TI     Cytokine receptor zcytor17
IN     Sprecher, Cindy A., Seattle, WA, UNITED STATES
       Presnell, Scott R., Tacoma, WA, UNITED STATES
       Gao, Zeren, Redmond, WA, UNITED STATES
       Whitmore, Theodore E., Redmond, WA, UNITED STATES
       Kuijper, Joseph L., Kenmore, WA, UNITED STATES
       Maurer, Mark F., Seattle, WA, UNITED STATES
PI     US 2003096339      A1   20030522
AI     US 2001-892949     A1   20010626 (9)
PRAI   US 2000-214282P     20000626 (60)
       US 2000-214955P     20000629 (60)
       US 2001-267963P     20010208 (60)
DT     Utility
FS     APPLICATION
LN.CNT 7977
INCL   INCLM: 435/069.100
       INCLS: 435/320.100; 435/325.000; 530/350.000; 536/023.500
NCL    NCLM:  435/069.100
       NCLS:  435/320.100; 435/325.000; 530/350.000; 536/023.500
IC     [7]
       ICM: C07K014-715
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1   ANSWER 6 OF 32  USPATFULL on STN
AN     2003:112973  USPATFULL
TI     Mouse cytokine receptor
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IN Presnell, Scott R., Tacoma, WA, UNITED STATES
Xu, Wenfeng, Mukilteo, WA, UNITED STATES
Kindsvogel, Wayne, Seattle, WA, UNITED STATES
Chen, Zhi, Bellevue, WA, UNITED STATES
PI US 2003077706 A1 20030424
AI US 2002-90365 A1 20020304 (10)
PRAI US 2001-273035P 20010302 (60)
US 2001-279232P 20010327 (60)
DT Utility
FS APPLICATION
LN.CNT 7834
INCL INCLM: 435/069.100
INCLS: 435/320.100; 435/325.000; 530/350.000; 536/023.500; 435/006.000
NCL NCLM: 435/069.100
NCLS: 435/320.100; 435/325.000; 530/350.000; 536/023.500; 435/006.000
IC [7]
ICM: A61K038-17
ICS: C07K014-715; C12Q001-68; C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 7 OF 32 USPATFULL on STN
AN 2003:102443 USPATFULL
TI Complementary DNA's encoding proteins with signal peptides
IN Edwards, Jean-Baptiste Dumas Milne, Paris, FRANCE
Bougueleret, Lydie, Vanves, FRANCE
Jobert, Severin, Paris, FRANCE
PA Genset, S.A., FRANCE (non-U.S. corporation)
PI US 6548633 B1 20030415
AI US 2000-599360 20000621 (9)
RLI Continuation-in-part of Ser. No. US 1999-469099, filed on 21 Dec 1999, now abandoned
PRAI US 1999-141032P 19990625 (60)
US 1998-113686P 19981222 (60)
DT Utility
FS GRANTED
LN.CNT 13743
INCL INCLM: 530/300.000
INCLS: 435/006.000; 536/023.100
NCL NCLM: 530/300.000
NCLS: 435/006.000; 536/023.100
IC [7]
ICM: A61K038-00
ICS: C12Q001-68; C07H021-02
EXF 435/6; 536/23.1; 530/300
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 8 OF 32 USPATFULL on STN
AN 2003:81593 USPATFULL
TI Purified and recombinant antigenic protein associated with abdominal aortic aneurysm (AAA) disease, and diagnostic and therapeutic use thereof
IN Tilson, Martin David, Scarsdale, NY, United States
PA The Trustees of Columbia University in the City of New York, New York, NY, United States (U.S. corporation)
PI US 6537769 B1 20030325
AI US 2000-535832 20000328 (9)
RLI Division of Ser. No. US 1997-812586, filed on 7 Mar 1997, now patented, Pat. No. US 6048704
PRAI US 1996-12976P 19960307 (60)
DT Utility
FS GRANTED
LN.CNT 3222

INCL INCLM: 435/007.900
INCLS: 435/007.100; 435/069.100; 435/069.300; 435/070.100; 436/501.000; 530/300.000; 530/350.000; 536/023.500
NCL NCLM: 435/007.900
NCLS: 435/007.100; 435/069.100; 435/069.300; 435/070.100; 436/501.000; 530/300.000; 530/350.000; 536/023.500
IC [7]
ICM: G01N033-53
ICS: G01N033-566; C07H021-04
EXF 435/7.1; 435/7.9; 435/69.1; 435/69.3; 435/70.1; 436/501; 530/300; 530/350; 536/23.5
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 9 OF 32 USPATFULL on STN
AN 2003:67830 USPATFULL
TI Four-helical bundle protein zsig81
IN Piddington, Christopher S., Thousand Oaks, CA, United States
West, James W., Seattle, WA, United States
Holly, Richard D., Seattle, WA, United States
Burkhead, Steven K., Hershey, PA, United States
PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6531576 B1 20030311
AI US 2000-585228 20000601 (9)
PRAI US 1999-137057P 19990601 (60)
DT Utility
FS GRANTED
LN.CNT 3953
INCL INCLM: 530/350.000
NCL NCLM: 530/350.000
IC [7]
ICM: C07K014-475
ICS: C07K014-47
EXF 530/350; 530/300; 530/326; 530/328; 514/12; 514/14; 514/15
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 10 OF 32 USPATFULL on STN
AN 2003:59938 USPATFULL
TI Growth factor homolog zvegf3
IN Gao, Zeren, Redmond, WA, United States
Hart, Charles E., Woodinville, WA, United States
Piddington, Christopher S., Thousand Oaks, CA, United States
Sheppard, Paul O., Granite Falls, WA, United States
Shoemaker, Kimberly E., Bellevue, WA, United States
Gilbertson, Debra G., Seattle, WA, United States
West, James W., Seattle, WA, United States
PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6528050 B1 20030304
AI US 2000-706968 20001106 (9)
RLI Continuation of Ser. No. US 2000-541752, filed on 31 Mar 2000
Continuation-in-part of Ser. No. US 1999-457066, filed on 7 Dec 1999
PRAI US 1999-165255P 19991112 (60)
US 1999-161653P 19991021 (60)
US 1999-142576P 19990706 (60)
US 1998-111173P 19981207 (60)
DT Utility
FS GRANTED
LN.CNT 4336
INCL INCLM: 424/085.100
INCLS: 424/198.100; 530/351.000; 530/399.000
NCL NCLM: 424/085.100
NCLS: 424/198.100; 530/351.000; 530/399.000
IC [7]

ICM: A61K045-00
EXF 424/85.1; 424/198.1; 530/351; 530/399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 11 OF 32 USPATFULL on STN
AN 2003:40660 USPATFULL
TI FGF homologs
IN Deisher, Theresa A., Seattle, WA, United States
Conklin, Darrell C., Seattle, WA, United States
Raymond, Fenella, Seattle, WA, United States
Bukowski, Thomas R., Seattle, WA, United States
Holderman, Susan D., Seattle, WA, United States
Hansen, Birgit, Seattle, WA, United States
Sheppard, Paul O., Redmond, WA, United States
PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6518236 B1 20030211
AI US 1999-229947 19990113 (9)
RLI Continuation-in-part of Ser. No. US 1997-951822, filed on 16 Oct 1997, now patented, Pat. No. US 5989866
PRAI US 1996-28646P 19961016 (60)
DT Utility
FS GRANTED
LN.CNT 3301
INCL INCLM: 514/002.000
INCLS: 514/012.000; 530/350.000; 530/399.000; 435/069.700
NCL NCLM: 514/002.000
NCLS: 435/069.700; 514/012.000; 530/350.000; 530/399.000
IC [7]
ICM: C07K014-50
ICS: A61K038-18
EXF 514/2; 514/12; 530/399; 530/350; 435/69.7
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 12 OF 32 USPATFULL on STN
AN 2003:37566 USPATFULL
TI **Fetuin**-MGP-mineral complex in serum
IN Price, Paul A., La Jolla, CA, UNITED STATES
PA The Regents of the University of California (U.S. corporation)
PI US 2003027211 A1 20030206
AI US 2001-45596 A1 20011018 (10)
RLI Continuation-in-part of Ser. No. US 2000-477505, filed on 4 Jan 2000, ABANDONED
DT Utility
FS APPLICATION
LN.CNT 3126
INCL INCLM: 435/007.100
INCLS: 435/013.000
NCL NCLM: 435/007.100
NCLS: 435/013.000
IC [7]
ICM: G01N033-53
ICS: C12Q001-56
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 13 OF 32 USPATFULL on STN
AN 2003:10656 USPATFULL
TI Novel FGF homologs
IN Deisher, Theresa A., Seattle, WA, UNITED STATES
Conklin, Darrell C., Seattle, WA, UNITED STATES
Raymond, Fenella C., Seattle, WA, UNITED STATES
Bukowski, Thomas R., Seattle, WA, UNITED STATES
Holderman, Susan D., Seattle, WA, UNITED STATES

Sheppard, Paul O., Redmond, WA, UNITED STATES
PA Zymogenetics, Inc. (U.S. corporation)
PI US 2003008351 A1 20030109
AI US 2002-81347 A1 20020221 (10)
RLI Continuation of Ser. No. US 1999-229947, filed on 13 Jan 1999, PENDING
PRAI US 1996-28646P 19961016 (60)
DT Utility
FS APPLICATION
LN.CNT 3583
INCL INCLM: 435/069.100
INCLS: 435/325.000; 435/320.100; 514/012.000; 530/350.000; 536/023.500
NCL NCLM: 435/069.100
NCLS: 435/325.000; 435/320.100; 514/012.000; 530/350.000; 536/023.500
IC [7]
ICM: C07K017-00
ICS: C07K014-00; C07K001-00; C12N005-02; C12N005-00; C12N015-74; C12N015-70; C12N015-63; C12N015-00; C12N015-09; C12P021-06; C07H021-04; A61K038-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 14 OF 32 USPATFULL on STN
AN 2002:332816 USPATFULL
TI Growth factor homolog ZVEGF4
IN Gilbert, Teresa, Seattle, WA, United States
Hart, Charles E., Woodinville, WA, United States
Sheppard, Paul O., Granite Falls, WA, United States
Gilbertson, Debra G., Seattle, WA, United States
PA Zymogenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6495668 B1 20021217
AI US 2000-564595 20000503 (9)
PRAI US 1999-132250P 19990503 (60)
US 1999-164463P 19991110 (60)
US 2000-180169P 20000204 (60)
DT Utility
FS GRANTED
LN.CNT 4816
INCL INCLM: 530/399.000
INCLS: 435/069.400; 435/070.100; 530/350.000; 536/023.400
NCL NCLM: 530/399.000
NCLS: 435/069.400; 435/070.100; 530/350.000; 536/023.400
IC [7]
ICM: A61K038-24
ICS: A61K038-27; C12N015-09; C07H021-04
EXF 435/69.4; 435/375; 435/377; 514/2; 530/350; 530/402; 530/387.1; 530/399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 15 OF 32 USPATFULL on STN
AN 2002:314716 USPATFULL
TI Growth factor homolog zvegf3
IN Gao, Zeren, Redmond, WA, UNITED STATES
Hart, Charles E., Woodinville, WA, UNITED STATES
Piddington, Christopher S., Thousand Oaks, CA, UNITED STATES
Sheppard, Paul O., Granite Falls, WA, UNITED STATES
Shoemaker, Kimberly E., Bellevue, WA, UNITED STATES
Gilbertson, Debra G., Seattle, WA, UNITED STATES
West, James W., Seattle, WA, UNITED STATES
PA Zymogenetics, Inc. (U.S. corporation)
PI US 2002177193 A1 20021128
AI US 2002-139583 A1 20020502 (10)
RLI Division of Ser. No. US 1999-457066, filed on 7 Dec 1999, PENDING
PRAI US 1998-111173P 19981207 (60)
US 1999-142576P 19990706 (60)

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       US 1999-161653P     19991021 (60)
       US 1999-165255P     19991112 (60)
DT     Utility
FS     APPLICATION
LN.CNT 5072
INCL   INCLM: 435/069.100
       INCLS: 435/320.100; 435/325.000; 530/399.000; 536/023.500
NCL    NCLM:  435/069.100
       NCLS:  435/320.100; 435/325.000; 530/399.000; 536/023.500
IC     [7]
       ICM: C07K014-475
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1   ANSWER 16 OF 32  USPATFULL on STN
AN     2002:213792  USPATFULL
TI     Novel protein zlmda2.
IN     Conklin, Darrell C., Seattle, WA, UNITED STATES
       Gao, Zeren, Redmond, WA, UNITED STATES
PI     US 2002115168      A1   20020822
AI     US 2001-990017     A1   20011121 (9)
PRAI   US 2000-252374P     20001121 (60)
DT     Utility
FS     APPLICATION
LN.CNT 2221
INCL   INCLM: 435/183.000
       INCLS: 435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.200
NCL    NCLM:  435/183.000
       NCLS:  435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.200
IC     [7]
       ICM: C12N009-00
       ICS: C07H021-04; C12P021-02; C12N005-06; C07K014-435
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1   ANSWER 17 OF 32  USPATFULL on STN
AN     2002:206162  USPATFULL
TI     Mammalian secreted proteins
IN     Sheppard, Paul O., Granite Falls, WA, UNITED STATES
       Presnell, Scott R., Tacoma, WA, UNITED STATES
PI     US 2002110855      A1   20020815
AI     US 2001-893737     A1   20010628 (9)
PRAI   US 2000-215446P     20000630 (60)
DT     Utility
FS     APPLICATION
LN.CNT 2681
INCL   INCLM: 435/069.100
       INCLS: 435/325.000; 435/320.100; 530/350.000; 530/391.100; 536/023.500
NCL    NCLM:  435/069.100
       NCLS:  435/325.000; 435/320.100; 530/350.000; 530/391.100; 536/023.500
IC     [7]
       ICM: C07K014-435
       ICS: C07K016-46; C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1   ANSWER 18 OF 32  USPATFULL on STN
AN     2002:201870  USPATFULL
TI     Growth factor homolog ZVEGF3
IN     Gao, Zeren, Redmond, WA, United States
       Hart, Charles E., Woodinville, WA, United States
       Piddington, Christopher S., Thousand Oaks, CA, United States
       Sheppard, Paul O., Granite Falls, WA, United States
       Shoemaker, Kimberly E., Bellevue, WA, United States
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Gilbertson, Debra G., Seattle, WA, United States
West, James W., Seattle, WA, United States
PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6432673 B1 20020813
AI US 1999-457066 19991207 (9)
PRAI US 1998-111173P 19981207 (60)
US 1999-142576P 19990706 (60)
US 1999-161653P 19991021 (60)
US 1999-165255P 19991112 (60)
DT Utility
FS GRANTED
LN.CNT 4888
INCL INCLM: 435/069.100
INCLS: 435/069.500; 435/006.000; 435/320.100; 435/325.000; 530/351.000; 530/399.000
NCL NCLM: 435/069.100
NCLS: 435/006.000; 435/069.500; 435/320.100; 435/325.000; 530/351.000; 530/399.000
IC [7]
ICM: C12N015-00
EXF 435/69.1; 435/69.5; 435/325; 530/351; 530/399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 19 OF 32 USPATFULL on STN
AN 2002:185650 USPATFULL
TI Novel core 2 beta-1,6-N-acetylglycosaminyltransferase gene
IN Korczak, Bozena, Toronto, CANADA
Lew, April, Toronto, CANADA
PI US 2002098563 A1 20020725
AI US 2001-797207 A1 20010302 (9)
RLI Continuation-in-part of Ser. No. US 2000-495913, filed on 2 Feb 2000, ABANDONED
PRAI US 1999-118674P 19990203 (60)
DT Utility
FS APPLICATION
LN.CNT 2504
INCL INCLM: 435/193.000
INCLS: 536/023.200; 435/320.100; 435/325.000; 435/069.100
NCL NCLM: 435/193.000
NCLS: 536/023.200; 435/320.100; 435/325.000; 435/069.100
IC [7]
ICM: C12N009-10
ICS: C07H021-04; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 20 OF 32 USPATFULL on STN
AN 2002:165355 USPATFULL
TI Full length expressed polynucleotides and the polypeptides they encode
IN Conklin, Darrell C., Seattle, WA, UNITED STATES
Presnell, Scott R., Tacoma, WA, UNITED STATES
Adler, David A., Bainbridge Island, WA, UNITED STATES
PI US 2002086988 A1 20020704
AI US 2001-800095 A1 20010305 (9)
PRAI US 2000-187221P 20000303 (60)
DT Utility
FS APPLICATION
LN.CNT 7304
INCL INCLM: 536/023.500
INCLS: 530/350.000; 435/006.000; 435/069.100; 435/325.000
NCL NCLM: 536/023.500
NCLS: 530/350.000; 435/006.000; 435/069.100; 435/325.000
IC [7]

ICM: C12Q001-68
ICS: C07H021-04; C12P021-02; C07K014-435
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 21 OF 32 USPATFULL on STN
AN 2002:164749 USPATFULL
TI Novel secreted proteins
IN Sheppard, Paul O., Granite Falls, WA, UNITED STATES
Presnell, Scott R., Tacoma, WA, UNITED STATES
Taft, David W., Seattle, WA, UNITED STATES
PI US 2002086367 A1 20020704
AI US 2001-895836 A1 20010629 (9)
PRAI US 2000-215446P 20000630 (60)
DT Utility
FS APPLICATION
LN.CNT 2511
INCL INCLM: 435/069.500
INCLS: 435/325.000; 435/320.100; 530/351.000; 530/388.230; 536/023.500
NCL NCLM: 435/069.500
NCLS: 435/325.000; 435/320.100; 530/351.000; 530/388.230; 536/023.500
IC [7]
ICM: C12P021-02
ICS: C07H021-04; C12N005-06; C07K014-52; C07K016-24
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 22 OF 32 USPATFULL on STN
AN 2002:157101 USPATFULL
TI Snake venom polypeptide zsnk1
IN Sheppard, Paul O., Granite Falls, WA, UNITED STATES
PI US 2002081700 A1 20020627
AI US 2001-923995 A1 20010807 (9)
PRAI US 2000-223164P 20000807 (60)
DT Utility
FS APPLICATION
LN.CNT 3778
INCL INCLM: 435/200.000
INCLS: 435/325.000; 536/023.200; 435/226.000; 435/320.100
NCL NCLM: 435/200.000
NCLS: 435/325.000; 536/023.200; 435/226.000; 435/320.100
IC [7]
ICM: C12N009-24
ICS: C12N009-64; C07H021-04
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 23 OF 32 USPATFULL on STN
AN 2002:148636 USPATFULL
TI Leucine-rich repeat proteins, Zlrr7, Zlrr8 and Zlrr9
IN Thayer, Edward C., Seattle, WA, UNITED STATES
Sheppard, Paul O., Granite Falls, WA, UNITED STATES
Presnell, Scott R., Tacoma, WA, UNITED STATES
PI US 2002076779 A1 20020620
AI US 2001-897214 A1 20010702 (9)
PRAI US 2000-215446P 20000630 (60)
DT Utility
FS APPLICATION
LN.CNT 3149
INCL INCLM: 435/183.000
INCLS: 435/325.000; 435/320.100; 530/388.100; 536/023.200; 435/069.100
NCL NCLM: 435/183.000
NCLS: 435/325.000; 435/320.100; 530/388.100; 536/023.200; 435/069.100
IC [7]
ICM: C12P021-02

ICS: C07H021-04; C07K016-42; C12N005-06; C12N009-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 24 OF 32 USPATFULL on STN
AN 2002:105951 USPATFULL
TI Zsig33-like peptides
IN Jaspers, Stephen R., Edmonds, WA, UNITED STATES
Sheppard, Paul O., Granite Falls, WA, UNITED STATES
Deisher, Theresa A., Seattle, WA, UNITED STATES
Bishop, Paul D., Fall City, WA, UNITED STATES
PI US 2002055156 A1 20020509
AI US 2001-853253 A1 20010510 (9)
PRAI US 2000-203300P 20000511 (60)
DT Utility
FS APPLICATION
LN.CNT 3022
INCL INCLM: 435/183.000
INCLS: 435/320.100; 435/325.000; 435/069.100; 536/023.200
NCL NCLM: 435/183.000
NCLS: 435/320.100; 435/325.000; 435/069.100; 536/023.200
IC [7]
ICM: C12N009-00
ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 25 OF 32 USPATFULL on STN
AN 2002:78709 USPATFULL
TI Method for treating inflammation
IN Thompson, Penny, Snohomish, WA, UNITED STATES
Foster, Donald C., Lake Forest Park, WA, UNITED STATES
Xu, Wenfeng, Mukilteo, WA, UNITED STATES
Madden, Karen L., Bellevue, WA, UNITED STATES
Kelly, James D., Mercer Island, WA, UNITED STATES
Sprecher, Cindy A., Seattle, WA, UNITED STATES
Blumberg, Hal, Seattle, WA, UNITED STATES
Eagan, Maribeth A., Seattle, WA, UNITED STATES
Jaspers, Stephen R., Edmonds, WA, UNITED STATES
Chandrasekher, Yasmin A., Mercer Island, WA, UNITED STATES
Novak, Julia E., Bainbridge Island, WA, UNITED STATES
PI US 2002042366 A1 20020411
US 6610286 B2 20030826
AI US 2000-746359 A1 20001222 (9)
PRAI US 1999-171969P 19991223 (60)
US 2000-213341P 20000622 (60)
DT Utility
FS APPLICATION
LN.CNT 3393
INCL INCLM: 514/012.000
INCLS: 424/145.100; 424/085.200
NCL NCLM: 424/085.200
NCLS: 424/085.100; 424/145.100; 514/012.000; 514/886.000; 530/350.000
IC [7]
ICM: A61K039-395
ICS: A61K038-20; A61K038-16
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 26 OF 32 USPATFULL on STN
AN 2002:72626 USPATFULL
TI Interferon-like protein Zcyto21
IN Sheppard, Paul O., Granite Falls, WA, UNITED STATES
Presnell, Scott R., Tacoma, WA, UNITED STATES
Fox, Brian A., Seattle, WA, UNITED STATES

Gilbert, Teresa, Seattle, WA, UNITED STATES
Haldeman, Betty A., Seattle, WA, UNITED STATES
Grant, Francis J., Seattle, WA, UNITED STATES
PI US 2002039763 A1 20020404
AI US 2001-895834 A1 20010629 (9)
PRAI US 2000-215446P 20000630 (60)
US 2001-285424P 20010420 (60)
DT Utility
FS APPLICATION
LN.CNT 3089
INCL INCLM: 435/069.100
INCLS: 435/325.000; 435/320.100; 435/183.000; 536/023.200
NCL NCLM: 435/069.100
NCLS: 435/325.000; 435/320.100; 435/183.000; 536/023.200
IC [7]
ICM: C12P021-02
ICS: C07H021-04; C12N009-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 27 OF 32 USPATFULL on STN
AN 2002:45596 USPATFULL
TI FGF Homologs
IN Deisher, Theresa A., Seattle, WA, United States
Conklin, Darrell C., Seattle, WA, United States
Raymond, Fenella, Seattle, WA, United States
Bukowski, Thomas R., Seattle, WA, United States
Holderman, Susan D., Kirkland, WA, United States
Hansen, Birgit, Seattle, WA, United States
Sheppard, Paul O., Redmond, WA, United States
PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6352971 B1 20020305
AI US 1999-368951 19990805 (9)
RLI Division of Ser. No. US 1997-951822, filed on 16 Oct 1997, now patented, Pat. No. US 5989866
PRAI US 1996-28646P 19961016 (60)
DT Utility
FS GRANTED
LN.CNT 2656
INCL INCLM: 514/002.000
INCLS: 435/007.100; 530/350.000; 530/387.100; 424/192.100
NCL NCLM: 514/002.000
NCLS: 424/192.100; 435/007.100; 530/350.000; 530/387.100
IC [7]
ICM: A61K038-00
ICS: A61K039-00; G01N033-53; C07K014-00; C07K016-00
EXF 530/300; 530/387.1; 435/7.1; 514/2; 424/192.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 28 OF 32 USPATFULL on STN
AN 2002:21834 USPATFULL
TI Human cytokine receptor
IN Presnell, Scott R, Tacoma, WA, UNITED STATES
Xu, Wenfeng, Mukilteo, WA, UNITED STATES
Kindsvogel, Wayne, Seattle, WA, UNITED STATES
Chen, Zhi, Seattle, WA, UNITED STATES
PI US 2002012669 A1 20020131
AI US 2000-728911 A1 20001201 (9)
PRAI US 1999-169049P 19991203 (60)
US 2000-232219P 20000913 (60)
US 2000-244610P 20001031 (60)
DT Utility
FS APPLICATION

LN.CNT 7478
INCL INCLM: 424/192.100
INCLS: 530/350.000; 536/023.500; 435/348.000; 435/326.000; 435/410.000; 435/252.100; 435/254.100; 435/255.100; 435/317.100; 435/069.100; 530/387.200; 530/388.100; 530/387.300; 530/389.100; 530/391.100; 514/012.000; 435/007.100; 435/006.000
NCL NCLM: 424/192.100
NCLS: 530/350.000; 536/023.500; 435/348.000; 435/326.000; 435/410.000; 435/252.100; 435/254.100; 435/255.100; 435/317.100; 435/069.100; 530/387.200; 530/388.100; 530/387.300; 530/389.100; 530/391.100; 514/012.000; 435/007.100; 435/006.000
IC [7]
ICM: A61K038-00
ICS: C12Q001-68; C07H021-04; A61K039-00; C12N001-20; C12N001-16; C12N001-14; C12N001-12; C12P021-06; G01N033-53
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 29 OF 32 USPATFULL on STN
AN 2002:16895 USPATFULL
TI Helical protein zalpha51
IN Conklin, Darrell C., Seattle, WA, UNITED STATES
Presnell, Scott R., Tacoma, WA, UNITED STATES
PI US 2002009775 A1 20020124
AI US 2001-810052 A1 20010316 (9)
PRAI US 2000-190410P 20000317 (60)
US 2000-199443P 20000425 (60)
DT Utility
FS APPLICATION
LN.CNT 3249
INCL INCLM: 435/069.100
INCLS: 435/006.000; 435/325.000; 530/350.000; 536/023.500; 435/320.100; 530/387.100; 435/007.100
NCL NCLM: 435/069.100
NCLS: 435/006.000; 435/325.000; 530/350.000; 536/023.500; 435/320.100; 530/387.100; 435/007.100
IC [7]
ICM: C12P021-02
ICS: C12Q001-68; C07H021-04; C12N005-06; G01N033-53; C12P021-06; C12N015-00; C12N015-09; C12N015-63; C12N015-70; C12N015-74; C12N005-00; C12N005-02; C07K001-00; C07K014-00; C07K017-00; C07K016-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 30 OF 32 USPATFULL on STN
AN 2000:43944 USPATFULL
TI Purified and recombinant antigenic protein associated with abdominal aortic aneurysm (AAA) disease, and diagnostic and therapeutic use thereof
IN Tilson, Martin David, Scarsdale, NY, United States
PA The Trustees of Columbia University, New York, NY, United States (U.S. corporation)
PI US 6048704 20000411
AI US 1997-812586 19970307 (8)
PRAI US 1996-12976P 19960307 (60)
DT Utility
FS Granted
LN.CNT 3522
INCL INCLM: 435/007.900
INCLS: 435/007.100; 435/069.100; 435/069.300; 435/070.100; 436/501.000; 536/023.500
NCL NCLM: 435/007.900
NCLS: 435/007.100; 435/069.100; 435/069.300; 435/070.100; 436/501.000; 536/023.500

IC [7]
ICM: G01N033-53
ICS: G01N033-566; C07H021-04
EXF 435/7.1; 435/7.9; 435/69.1; 435/69.3; 435/70.1; 436/501; 536/23.5
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 31 OF 32 USPATFULL on STN
AN 1999:150969 USPATFULL
TI FGF homologs
IN Deisher, Theresa A., Seattle, WA, United States
Conklin, Darrell C., Seattle, WA, United States
Raymond, Fenella, Seattle, WA, United States
Bukowski, Thomas R., Seattle, WA, United States
Holderman, Susan D., Kirkland, WA, United States
Hansen, Birgit, Seattle, WA, United States
Sheppard, Paul O., Redmond, WA, United States
PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 5989866 19991123
AI US 1997-951822 19971016 (8)
PRAI US 1996-28646P 19961016 (60)
DT Utility
FS Granted
LN.CNT 2660
INCL INCLM: 435/069.400
INCLS: 435/243.000; 435/320.100; 435/325.000; 536/023.510; 935/013.000
NCL NCLM: 435/069.400
NCLS: 435/243.000; 435/320.100; 435/325.000; 536/023.510
IC [6]
ICM: C12N015-18
ICS: C12N015-63; C12N001-21; C12N005-00
EXF 435/69.4; 435/320.1; 435/70.1; 435/325; 435/243; 536/23.51; 935/13
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 32 OF 32 USPATFULL on STN
AN 88:14530 USPATFULL
TI Method for adsorbing and desorbing
IN Itoh, Hiroshi, Yokohama, Japan
Nakagawa, Toshimi, Fujisawa, Japan
Nitta, Atsuhiko, Yokohama, Japan
Tanaka, Tomio, Tokyo, Japan
Kamio, Hideo, Odawara, Japan
Nagai, Katsutoshi, Yonezawa, Japan
PA Mitsui Toatsu Chemicals, Inc., Tokyo, Japan (non-U.S. corporation)
PI US 4729834 19880308
AI US 1986-878647 19860626 (6)
RLI Continuation-in-part of Ser. No. US 1985-728211, filed on 29 Apr 1985, now abandoned And Ser. No. US 1985-728027, filed on 29 Apr 1985, now abandoned
PRAI JP 1984-89386 19840507
JP 1984-89315 19840507
JP 1984-106466 19840528
DT Utility
FS Granted
LN.CNT 1374
INCL INCLM: 210/670.000
INCLS: 210/692.000
NCL NCLM: 210/670.000
NCLS: 210/692.000
IC [4]
ICM: B01D015-00
EXF 210/670; 210/692
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> s l1 and risk
        225672 RISK
L2           9 L1 AND RISK

=> d l2 1-9 bib, ab,  kwic

L2   ANSWER 1 OF 9  USPATFULL on STN
AN     2003:206834  USPATFULL
TI     Chemokine beta-1 fusion proteins
IN     Bell, Adam, Germantown, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
PI     US 2003143191      A1   20030731
AI     US 2002-153604     A1   20020524 (10)
PRAI   US 2001-293212P     20010525 (60)
DT     Utility
FS     APPLICATION
LREP   HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN   Number of Claims: 17
ECL    Exemplary Claim: 1
DRWN   21 Drawing Page(s)
LN.CNT 15446
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     The present invention relates to novel chemokine polypeptides and
       encoding nucleic acids. More specifically, therapeutic compositions and
       methods are provided using isolated nucleic acid molecules encoding a
       human chemokine beta-1 (Ck.beta.-1 or Ckb1) polypeptide (previously
       termed monocyte-colony inhibitory factor (M-CIF), MIP1-.gamma., and
       Hemofiltrate CC chemokine-1 (HCC-1)), and Ckb1 polypeptides themselves,
       as are vectors, host cells and recombinant methods for producing the
       same. Also provided are methods of treating, preventing, ameliorating
       diseases using such compounds.
DETD   . . . fusion proteins) and/or polynucleotides of the invention is
       contemplated for the prevention of occulsion of saphenous grafts, for
       reducing the risk of periprocedural thrombosis as might
       accompany angioplasty procedures, for reducing the risk of
       stroke in patients with atrial fibrillation including nonrheumatic
       atrial fibrillation, for reducing the risk of embolism
       associated with mechanical heart valves and or mitral valves disease.
       Other uses for the therapeutics of the invention,. . .
DETD   . . . albumin fusion proteins) of the invention may be used for the
       prevention of occulsion of saphenous grafts, for reducing the
       risk of periprocedural thrombosis as might accompany angioplasty
       procedures, for reducing the risk of stroke in patients with
       atrial fibrillation including nonrheumatic atrial fibrillation, for
       reducing the risk of embolism associated with mechanical heart
       valves and or mitral valves disease. Other uses for the fusion proteins
       (e.g. albumin. . .
DETD   . . . by affinity chromatography on a Blue Sepharose FF column using
       a salt gradient elution. Blue Sepharose FF removes the main BSA/
       fetuin contaminants. Further purification over the Poros PI 50
       resin with a phosphate gradient may remove and lower endotoxin
       contamination as. . .
DETD   . . . arthritis, diabetes, inflammatory skin conditions, psoriasis,
       eczema, systemic lupus erythematosus, multiple sclerosis,
       glomerulonephritis, inflammatory bowel disease, crohn's disease,
       ulcerative colitis, arteriosclerosis, cirrhosis, graft vs.
       host disease, host vs. graft disease, hepatitis, leukemia and lymphoma.

L2   ANSWER 2 OF 9  USPATFULL on STN
AN     2003:102443  USPATFULL
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TI Complementary DNA's encoding proteins with signal peptides
IN Edwards, Jean-Baptiste Dumas Milne, Paris, FRANCE
Bougueleret, Lydie, Vanves, FRANCE
Jobert, Severin, Paris, FRANCE
PA Genset, S.A., FRANCE (non-U.S. corporation)
PI US 6548633 B1 20030415
AI US 2000-599360 20000621 (9)
RLI Continuation-in-part of Ser. No. US 1999-469099, filed on 21 Dec 1999, now abandoned
PRAI US 1999-141032P 19990625 (60)
US 1998-113686P 19981222 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Horlick, Kenneth R.; Assistant Examiner: Kim, Young
LREP Saliwanchik, Lloyd & Saliwanchik
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 13743
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The sequences of cDNAs encoding secreted proteins are disclosed. The cDNAs can be used to express secreted proteins or fragments thereof or to obtain antibodies capable of specifically binding to the secreted proteins. The cDNAs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. The cDNAs may also be used to design expression vectors and secretion vectors.
SUMM . . . a consequence of a mutation in the coding sequence for a secreted protein. In instances where the individual is at **risk** of suffering from a disease or other undesirable phenotype as a result of a mutation in such a coding sequence,. . .
DETD . . . Their functions include control of endocytosis, cell proliferation and differentiation, immune response, bone formation and resorption, and apoptosis. More specifically, **fetuin** levels in human plasma are regulated in the manner of a negative acute phase reactant (Lebreton et al., J. Clin.. . . decline in some cancer patients correlating with impaired cellular immune function (Baskies et al., Cancer 45:3050-58 (1980)). During mouse embryogenesis, **fetuin** mRNA is expressed in a number of developing organs and tissues including the heart, kidney, lung, nervous system and liver (Yang et al., Biochem. Biophysic. Acta 1130:149-56 (1992)). Mammalian **fetuin** present in sub-populations of neurons in the developing central and peripheral nervous system is associated to cell survival (Saunders et al., Anat. Embryol 186:477-86 (1992)); Kitchener et al., Int J. Dev. Neurosci. 15:717-27 (1997)). **Fetuin** is able to promote growth in tissue culture (Puck et al. Proc. Natl. Acad. Sci. U.S.A., 59:192-99 (1968)), to enhance. . . and to stimulate adipogenesis in cell culture models (Cayatte et al., J. Biol. Chem. 265:5883-8 (1990)). Abnormal serum levels of **fetuin** are associated with alteration in cellular and biochemical properties of bone, Paget's disease, reduced bone quality and osteogenesis imperfecta (for a review see Binkert et al, J. Biol. Chem. 274:28514-20 (1999)). Part of the **fetuin** activities has been shown to depend upon their ability to inhibit the activity of TGF-beta cytokines and bone morphogenetic proteins. . .
DETD . . . reactions and immune cell mediated injuries. Such injuries include, but are not limited to, adult respiratory distress syndrome, allergies, asthma, **arteriosclerosis**, bronchitis, emphysema, hypereosinophilia, myocardial or pericardial inflammation, rheumatoid arthritis, complications of heart attack, stroke, cancer, hemodialysis, infections, and trauma.

L2 ANSWER 3 OF 9 USPATFULL on STN

AN 2003:81593 USPATFULL
TI Purified and recombinant antigenic protein associated with abdominal aortic aneurysm (AAA) disease, and diagnostic and therapeutic use thereof
IN Tilson, Martin David, Scarsdale, NY, United States
PA The Trustees of Columbia University in the City of New York, New York, NY, United States (U.S. corporation)
PI US 6537769 B1 20030325
AI US 2000-535832 20000328 (9)
RLI Division of Ser. No. US 1997-812586, filed on 7 Mar 1997, now patented, Pat. No. US 6048704
PRAI US 1996-12976P 19960307 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Swartz, Rodney P
LREP White, John P., Cooper & Dunham LLP
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 44 Drawing Figure(s); 24 Drawing Page(s)
LN.CNT 3222
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides an isolated protein of approximately 40 kDa which is purified from human aortic tissue and immunoreactive with AAA-associated immunoglobulin. Also provided are a method of diagnosing AAA disease in a subject using said isolated protein and a pharmaceutical composition comprising said isolated protein. A method of alleviating AAA disease in a subject comprising administering said pharmaceutical composition comprising the isolated protein is also provided. The subject invention also provides a recombinantly produced human aortic protein which is immunoreactive with AAA-associated immunoglobulin. Also provided are a method of diagnosing AAA disease in a subject using said recombinantly produced protein and a pharmaceutical composition comprising said recombinantly produced protein. A method of alleviating AAA disease in a subject comprising administering said pharmaceutical composition comprising the recombinantly produced protein is also provided.
DRWD . . . Control glycoprotein transferrin (TRNSF) reacted with SNA, indicating sialic acid terminally linked alpha (2-6) to galactose or N-acetylgalactosamine. Control glycoprotein **fetuin** (FETN) reacted with SNA, MAA (indicating sialic acid terminally linked alpha (2-3) to galactose), and DSA (indicating galactose beta (1-4). . .
DETD 7. DePalma R G, Sidaway A N, Giordana J M. Associated aetiological and atherosclerotic **risk** factors in abdominal aneurysms. in: The Cause and Management of Aneurysms, ed. R M Greenhalgh, J A Mannick, J T. . .
DETD . . . H, Nagase H, Tilson M D. Identification of matrix metalloproteinases 3 (stromelysin-1) and 9 (gelatinase B) in abdominal aortic aneurysm. **Arteriosclerosis** and Thrombosis, 1994; 14: 1315-1320.

L2 ANSWER 4 OF 9 USPATFULL on STN
AN 2003:40660 USPATFULL
TI FGF homologs
IN Deisher, Theresa A., Seattle, WA, United States
Conklin, Darrell C., Seattle, WA, United States
Raymond, Fenella, Seattle, WA, United States
Bukowski, Thomas R., Seattle, WA, United States
Holderman, Susan D., Seattle, WA, United States
Hansen, Birgit, Seattle, WA, United States
Sheppard, Paul O., Redmond, WA, United States
PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6518236 B1 20030211

AI US 1999-229947 19990113 (9)
RLI Continuation-in-part of Ser. No. US 1997-951822, filed on 16 Oct 1997, now patented, Pat. No. US 5989866
PRAI US 1996-28646P 19961016 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Saoud, Christine J.
LREP Sawislak, Deborah A.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 3301
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to polynucleotide and polypeptide molecules for zFGF5 a novel member of the FGF family. The polypeptides, and polynucleotides encoding them, are proliferative for muscle cells, in particular cardiac cells and may be used for remodeling cardiac tissue and improving cardiac function. The present invention also includes antibodies to the zFGF5 polypeptides.
SUMM . . . accounts for 750,000 hospital admissions per year in the U.S., with more than 5 million people diagnosed with coronary disease. **Risk** factors for MI include diabetes mellitus, hypertension, truncal obesity, smoking, high levels of low density lipoprotein in the plasma or. . .
DETD . . . mg/ml L-glutamine (Sigma, St. Louis, MO)
1 mM sodium pyruvate (Sigma, St. Louis, MO)
25 mM Hepes (Sigma, St. Louis, MO)
10 .mu.g/ml **fetuin** (Aldrich, Milwaukee, WI)
50 .mu.g/ml insulin (Gibco-BRL)
3 ng/ml selenium (Aldrich, Milwaukee, WI)
20 .mu.g/ml transferrin (JRH, Lenexa, KS)
DETD . . . circulation. High levels of expression and physiological effects have been demonstrated (Ohwada et al., Blood 88:768-774, 1996; Stevenson et al., **Arteriosclerosis**, Thrombosis and Vascular Biology, 15:479-484, 1995; Setoguchi et al., Blood 84:2946-2953, 1994; and Sakamoto et al., Proc. Natl. Acad. Sci.. . .
DETD . . . using Lipofectamine.TM. (Gibco BRL), in serum free (SF) media formulation (Ham's F12, 10 mg/ml transferrin, 5 mg/ml insulin, 2 mg/ml **fetuin**, 1% L-glutamine and 1% sodium pyruvate). ZFGF5/pZMP6 is diluted into 15 ml tubes to a total final volume of 640. . .

L2 ANSWER 5 OF 9 USPATFULL on STN
AN 2003:37566 USPATFULL
TI **Fetuin**-MGP-mineral complex in serum
IN Price, Paul A., La Jolla, CA, UNITED STATES
PA The Regents of the University of California (U.S. corporation)
PI US 2003027211 A1 20030206
AI US 2001-45596 A1 20011018 (10)
RLI Continuation-in-part of Ser. No. US 2000-477505, filed on 4 Jan 2000, ABANDONED
DT Utility
FS APPLICATION
LREP QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C., P O BOX 458, ALAMEDA, CA, 94501
CLMN Number of Claims: 75
ECL Exemplary Claim: 1
DRWN 20 Drawing Page(s)
LN.CNT 3126
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods of inhibiting calcification of a soft tissue (e.g., an artery, a heart valve, an atherosclerotic plaque, a cancer, a kidney, a prostate, skin, muscle, cartilage, viscera, and

heart muscle) in a mammal. These methods involve inhibiting osteoclastic bone resorption in said mammal (e.g., a mammal diagnosed as having or at **risk** for a pathology characterized by calcification of a soft tissue). The inhibition is preferably by administration of a bisphosphonate to the mammal in a concentration sufficient to inhibit bone resorption without inhibiting bone mineralization. The methods of this invention can also be used to mitigate a symptom of atherosclerosis in a mammal. Such methods involve inhibiting osteoclastic bone resorption in the mammal. In preferred embodiment, the inhibiting is by administration of a bisphosphonate to the mammal in a concentration sufficient to inhibit bone resorption without inhibiting bone mineralization

TI **Fetuin**-MGP-mineral complex in serum

AB . . . a mammal. These methods involve inhibiting osteoclastic bone resorption in said mammal (e.g., a mammal diagnosed as having or at **risk** for a pathology characterized by calcification of a soft tissue). The inhibition is preferably by administration of a bisphosphonate to. . .

SUMM . . . discovery that agents that inhibit bone resorption will also inhibit ectopic calcification and/or plaque formation and related pathologies associated with **arteriosclerosis**. Without being bound to a particular theory, it is believed that the process of bone resorption, delivers solubilized calcium (e.g.. . .

SUMM . . . a mammal. These methods involve inhibiting osteoclastic bone resorption in said mammal (e.g., a mammal diagnosed as having or at **risk** for a pathology characterized by calcification of a soft tissue) The inhibition is preferably by administration of a bisphosphonate to. . .

SUMM . . . cancer, a kidney, a prostate, skin, muscle, cartilage, viscera, and heart muscle) in a mammal diagnosed as having or at **risk** for a pathology characterized by calcification of a soft tissue. These methods involve administering to the animal a low dosage. . .

SUMM . . . soft tissue without inhibiting bone calcification. Such diseases include, but are not limited to atherosclerosis, arteriosclerosis, arteriolosclerosis, hypertensive arteriolosclerosis, Monckeberg's **arteriosclerosis**, heart valve stenosis, uremia, diabetes, hyperparathyroidism, blood clot formation, cancer growth, cancer metastasis, hypertension, vitamin D toxicity, and arthritis. Preferred. . . but are not limited to the bisphosphonates and dosages described above. The mammal may be diagnosed as having or at **risk** for a pathology characterized by calcification of a soft tissue.

SUMM . . . bone resorption without inhibiting bone mineralization. Preferred mammals include, but are not limited to mammals diagnosed as having, or at **risk** for, atherosclerosis. Preferred bisphosphonates and dosages include, but are not limited to the bisphosphonates and dosages described above. The bisphosphonate. . .

SUMM . . . of calcium or a calcium salt in an aqueous phase. These methods involve contacting the calcium or calcium salt with **fetuin**.

SUMM . . . The stabilized calcium provides a method of delivering a calcification initiator to a preselected site. Such methods involve providing a **fetuin**-mineral complex attached to a targeting molecule (e.g., antibody, lectin, nucleic acid etc.) where the targeting molecule specifically binds to the preselected site; and contacting the **fetuin** mineral complex to the preselected site.

SUMM . . . Also provided is a method of distributing mineral nuclei within a matrix. This method involves impregnating the matrix with a **fetuin**-mineral complex and denaturing the **fetuin** such that the mineral is released from the **fetuin** mineral complex.

SUMM [0023] The **fetuin** can also be used to stabilize the size or crystal structure of a mineral salt in an aqueous phase. This method involves contacting the mineral salt with a **fetuin**.

SUMM [0024] This invention also provides substantially isolated mineral salts (e.g. calcium phosphate) stabilized in a complex with **fetuin**.

SUMM [0035] The following abbreviations used are: MGP, matrix Gla protein; BGP, bone Gla protein (osteocalcin); **fetuin**, .alpha.2-HS Glycoprotein; and Gla, .gamma.-Carboxyglutamic Acid.

DETD . . . the methods of this invention are particularly applicable in two contexts: 1) Where the organism (animal or human) is at **risk** for or has an ectopic calcification; and 2) Where the organism (animal or human) is at **risk** for, or has, atherosclerosis or **arteriosclerosis**.

DETD . . . embodiment the methods of this invention are used for the treatment (therapeutic or prophylactic) of an organism having, or at **risk** for, a calcification of a soft tissue. As used herein, a "soft tissue" refers to a tissue that is not. . .

DETD . . . failure is very high, over 75%, and essentially all stenotic valves fail because of calcification. The number of subjects at **risk** for stenosis and heart valve replacement is fairly high, since it includes all subjects with some extent of heart valve calcification, which is about 30% of human subjects in their 60s. This high incidence of **risk** for stenoses suggests that the methods of this invention could be used prophylactically to decrease the **risk** of heart valve failure in all subjects for which there is evidence of progressive valve calcification.

DETD [0068] B) Atherosclerosis and **Arteriosclerosis**.

DETD [0069] As indicated above, the methods of this invention are applicable to mammals (e.g. humans) having, or at **risk** for, atherosclerosis. Atherosclerosis refers to a progressive narrowing and hardening of the arteries over time. More generally, the methods of this invention are applicable to any **arteriosclerosis** that involves the deposition of calcium in the vascular intima. Thus, the methods of this invention are applicable to atheroscleroses. . . non-atheromatous arterioscleroses involving calcium deposition including, but not limited to Diabetes mellitus, chronic renal insufficiency, chronic vitamin D intoxication, Monckeberg's **arteriosclerosis**, **arteriosclerosis**, hypertensive **arteriosclerosis**, pseudoxanthoma elasticum, idiopathic arterial calcification in infancy, aortic valvular calcification in the elderly, and Werner's syndrome.

DETD [0070] Differential diagnoses for these conditions and/or for **risk** of these conditions are well known to medical personnel.

DETD [0094] V. **Fetuin** Complexes.

DETD [0095] It was also a discovery of this invention that the serum protein **fetuin** forms a stable complex with a calcium phosphate mineral phase and that this complex can under some circumstances be detected in blood. Without being bound to a particular theory it is believed that the **fetuin**/calcium phosphate complex is a form in which calcium removed during bone resorption is solubilized in plasma and migrates to new. . .

DETD [0096] The **fetuin**-mineral complex can be synthesized using pure **fetuin**, calcium, and phosphate (see, Example 2). In brief, the procedure allows the synthesis of small mineral particles of uniform size which can be seen by transmission electron microscopy. Because the size of the **fetuin** mineral complex is very small, a solution containing very high concentrations of the **fetuin** mineral complex is quite clear and the complex does not settle. The particles are stable, with no apparent changes over. . .

DETD . . . dense white precipitate forms within a fraction of a second which slowly sinks to the bottom the test tube. If **fetuin** is added prior to mixing, the dense white precipitate fails to form and the solution remains quite clear for days.. . . microscopy, numerous small mineral nuclei are present which have remarkably uniform size and shape. The nuclei, which are coated with **fetuin**, account for

over 95% of the calcium and phosphate in the mixture. This experiment illustrates the power of the **fetuin** molecule to direct the course of a mineralization process.

DETD . . . this mineral phase selectively in order to trap the unstable phase and prevent its transformation to more stable phases. A **fetuin** mineral complex can be used to distribute mineral nuclei within a suitable matrix so that subsequent inactivation of **fetuin** (e.g. by heat, acid, addition of a chaotropic agent, etc.) would cause rapid and uniform calcification of this matrix. This. . .

DETD [0099] Because the **fetuin** mineral complex is stable in blood, it can be used as a transport vehicle to deliver calcification initiators to desired sites in the body. For example, the **fetuin** in the complex could be modified so that it binds to a site where calcification is desired (e.g. teeth, bone, etc.) and so that **fetuin** can be inactivated at this site to allow mineralization to proceed. Typically such a modification would involve coupling a targeting. . . molecule (e.g., an antibody, antibody fragment, single chain antibody, a lectin, a lipid, a carbohydrate, a sugar, etc.) to the **fetuin**-mineral complex. The targeting molecule is selected to specifically bind to the target (e.g. cell receptor, ligand, etc.) whereby the mineral. . .

DETD [0100] It is noted that **fetuin** is a glycoprotein and methods of attaching molecules to glycoproteins (directly or through a linker) are well known to those. . . a linker. A "linker" as used herein, is a molecule that is used to join the targeting molecule to the **fetuin**-mineral complex. The linker is capable of forming covalent bonds to both the **fetuin** and to the targeting molecule. Suitable linkers are well known to those of skill in the art and include, but. . .

DETD [0102] The **fetuin** mineral complex can also be used as a reagent to develop **fetuin**-mineral specific assays which, in turn, can be used to determine the levels of a **fetuin** mineral complex in human blood. This would provide a method to measure bone metabolic processes relevant to the management of. . .

DETD [0103] Without being bound to a particular theory, it is believed that a surface of the **fetuin** molecule binds strongly and specifically to the target mineral phase. This binding exposes surfaces on **fetuin** which have a high affinity for other bound **fetuin** molecules, forming strong lateral associations that arrest crystal growth. The oligosaccharide moieties in **fetuin**, which account for about half of its mass, project away from mineral and form a hydrated shell which keeps the **fetuin** mineral complex from aggregating or settling from solution. This model suggests that engineered modifications in the mineral interaction surface of **fetuin** could direct the protein to any desired mineral phase, thereby enabling the protein to control the synthesis of this mineral. . .

DETD [0104] VI. **Fetuin** Complexes as Prognostic Markers, Diagnostic Markers, and Surrogate Markers.

DETD [0105] In still another embodiment, this invention pertains to the discovery that the **fetuin**-mineral complex in blood (e.g. serum), is an effective prognostic and diagnostic marker for calcification of arteries and other soft tissues, atherosclerosis, and osteoporosis. In general, increased levels (e.g. increased serum concentration) of the **fetuin**-mineral complex in a mammal indicates that the mammal is at increased **risk** for or has calcification of arteries and/or other soft tissues, and/or atherosclerosis, and/or osteoporosis.

DETD [0106] When used as a prognostic or diagnostic marker, the **fetuin**-mineral complex level (serum concentration) is preferably used in the context of a differential diagnosis or prognosis for

presence or **risk** of atherosclerosis, soft tissue calcification and/or osteoporosis. When used in the context of other known diagnostic markers and/or **risk** factors for each of these conditions, it is possible to determine for which condition, or combination of conditions, the **fetuin** mineral complex is an indicator.

DETD [0107] The **fetuin**-mineral complex also provides a convenient marker for the response of an organism for treatment. In this context, a mammal (e.g. a human or non-human mammal) having one or more of the above-identified conditions is treated for those condition(s). The **fetuin**-mineral complex level in the mammal (e.g. in a blood sample from the mammal) is monitored before and/or during and/or after the treatment. A decrease in the level of the **fetuin** mineral complex (preferably a statistically significant decrease) indicates that the mammal is responding to the treatment.

DETD [0108] The decrease in **fetuin**-mineral complex, is typically evaluated with respect to a control. Suitable controls include, but are not limited to blood from the. . . from the same mammal obtained at an earlier time point in the course of the treatment, the level of a **fetuin**-mineral complex found in a normal healthy mammal of the same species, a predetermined concentration of a **fetuin** -mineral complex, and the like.

DETD [0109] Methods of detecting and/or isolating the **fetuin** mineral complex are detailed in Example 3. Using the methods described therein, one of skill can readily optimize protocols to facilitate **fetuin**-mineral complex isolation from essentially any mammalian species including humans. Thus, for example, in one particularly preferred embodiment, when isolating the **fetuin** mineral complex from humans the **fetuin**-mineral complex is sedimented by using high centrifugational speeds and relatively long centrifugation times. The following is an example of a. . .

DETD . . . the side away from the axis of rotation, since this is the side that will have the pellet containing the **fetuin** mineral complex. The tube is centrifuged for a total of 1 h at 110,000 rpm. The supernatant is then removed. . . and gently tapped on a kimwipe to remove any remaining supernatant. The airfuge tube is checked to see if a **fetuin**-mineral complex can be detected. If there is a substantial amount of the **fetuin**-mineral complex it can be seen as a small glassy pellet on the bottom side of the tube furthest from the. . . of 0.15M HCl is added to the tube and incubated 1 h at room temperature in order to dissolve the **fetuin**-mineral complex. The level of calcium, and/or phosphate, and/or MGP, and/or **fetuin** can be determined in the dissolved pellet. The amount of **fetuin**-mineral complex can be calculated from the amount of any of these constituents that are found in the pellet. The level of calcium, and/or phosphate, and/or MGP, and/or **fetuin** in the supernatant and in the original sample is determined. If a substantial amount of the complex is present, there. . .

DETD [0112] Detection of low levels of the **fetuin** mineral complex may be hampered by the presence of small amounts of serum that wet the tube even after the supernatant is removed, since the supernatant will contain calcium, phosphate, MGP, and **fetuin**. To control for this problem, set up an identical tube of the sample but skip step the centrifugation step. The amount of calcium, phosphate, MGP, and/or **fetuin** in this acid extract can then be subtracted from the amount present in the tube that was centrifuged. An alternative. . . of 0.15M HCl is added to the tube and incubated 1 h at room temperature in order to dissolve the **fetuin**-mineral complex as described above.

DETD . . . to provide a measure of the amount of the complex present. Such consitutents include, but are not limited to the **fetuin**, matrix Gla protein, secreted phosphoprotein 24, platelet factor 4, calcium, phosphate, mineral phase, and the like.

DETD [0116] In another embodiment, this invention provides kits for the presence or likelihood (**risk** for) atherosclerosis, and/or calcification of an artery or other soft tissue, and/or osteoporosis. The kits typically comprise one or more reagents used in the isolation and/or detection of a **fetuin** mineral complex (e.g. as described in Example 3). The kit, optionally, also includes instructional materials providing protocols for the isolation and/or detection (e.g. quantification) of a **fetuin**-mineral complex.

DETD [0156] Artery calcification is associated with **arteriosclerosis**, a term which is derived in part from the Greek word for hardness, sklerosis. **Arteriosclerosis** refers to hardening of arteries, and the types of **arteriosclerosis** include atherosclerosis, Monckeberg's **arteriosclerosis**, hypertensive **arteriosclerosis**, and arteriolosclerosis. Atherosclerosis is the most prevalent **arteriosclerosis**, and calcification is typically associated with the atherosclerotic plaque itself. While the relationship between calcification and the progression of atherosclerosis. . .

DETD [0158] **Arteriosclerosis** is also frequently associated with uremia and, in dialysis patients, the frequency of artery calcification increases with the duration of. . . Dermatol. 33:954-962). A recent study of 7,096 hemodialysis patients has identified the serum calcium X phosphate product as an independent **risk** factor for death, with a relative mortality **risk** of 1.34 (Block et al. (1998) Am. J. Kidney Diseases. 31: 607-617). While the mechanism by which the serum calcium. . .

DETD Synthesis and Use of a **Fetuin**-Mineral Comples

DETD [0162] We discovered the existence of a complex between a calcium phosphate mineral phase and the serum protein **fetuin** in the course of investigating the effects of high etidronate doses on the chemical composition of serum in rats. To. . .

DETD [0163] In a preferred embodiment, the creation of a **fetuin** mineral complex involves the creation of a solution which is supersaturated with respect to the calcium phosphate mineral phase. This is done in the presence of **fetuin** at physiological pH (that is, pH values found in serum). In the two procedures outlined below, we have generated the. . . mineral nuclei by a homogeneous nucleation process. It was one of the discoveries of this research that the presence of **fetuin** arrests the growth and aggregation of the mineral phase so that many small crystallites are formed. Since the size of. . . itself remains clear for many days at room temperature in spite of the presence of rather large amounts of the **fetuin** mineral complex.

DETD [0165] Procedure for the Preparation of **Fetuin** Mineral Complex Using Fetal Calf Serum, Calcium, and Phosphate.

DETD [0166] A first approach to preparing a **fetuin**-mineral complex uses fetal calf serum. The fetal calf serum is brought and about 2 ML is aliquoted into a test. . .

DETD [0169] Procedure for the Preparation of the **Fetuin** Mineral Complex Using Purified Bovine **Fetuin**, Calcium, and Phosphate.

DETD [0170] A second approach to preparing a **fetuin**-mineral complex uses purified bovine **fetuin**, calcium, and phosphate fetal calf serum. First, 50 mg of purified bovine **fetuin** are dissolved in 2.5 mL of 0.2M HEPES pH 7.4. The mixture is spun at top speed for 30 minutes in an epifuge to clarify the solution. (The Sigma **fetuin** we use in these experiments contains a small portion of protein which does not dissolve in this buffer.) About 160. . . into a 12.times.75 tube. In a separate 12.times.75 tube is placed 80 .mu.l of 1M CaCl.sub.2. 1 mL of the **fetuin**-HEPES buffer solution prepared in step 2 is rapidly added to both tubes.

DETD . . . structure to those formed after 3 h at room temperature in the experiments outlined above. We have also formed the **fetuin**

mineral complex using initial molar ratios of calcium to phosphate ranging from 2:1 to 0.5:1, and find that the final. . .

DETD [0176] The **fetuin** mineral complexes formed by the above procedures can be sedimented by centrifugation for 5 to 30 minutes at high speed in an epifuge. The pellet which forms is translucent and glassy in appearance, and contains **fetuin**, calcium, and phosphate. The molar ratio of calcium to phosphate in this complex is about 1.25 and the weight ratio of **fetuin** to calcium in this complex is about 3.

DETD [0178] The initial concentration of purified bovine **fetuin** can be varied. We have successfully formed the **fetuin** mineral complex using **fetuin** at 5 mg/ml and an initial ion composition of 10 mM calcium and phosphate, and using **fetuin** at 1 mg/ml and an initial ion composition of 5 mM calcium and phosphate. In general, less **fetuin** is required to form a stable complex of uniform size and structure at lower initial concentrations of calcium and phosphate.

DETD [0179] The species source of **fetuin** can be varied. While we have not investigated complex formation using purified **fetuin** from other species, we have successfully formed the **fetuin** mineral complex using rat and human serum starting with initial calcium and phosphate concentrations of 10 mM. (Human **fetuin** is also called .alpha.2-HS Glycoprotein.)

DETD . . . homogeneous nucleation conditions using a low initial ion concentrations, and it is therefore these conditions which favor the formation of **fetuin** mineral complexes which are the most uniform in structure.

DETD A **Fetuin**-MGP-Mineral Complex in Serum

DETD . . . that inhibit normal bone mineralization. The composition of this high molecular weight protein-mineral complex consists of about 18% mineral, 80% **fetuin**, and 2% matrix Gla protein (MGP) by weight, and the presence of the complex in serum after an injection of. . . . h following subcutaneous injection of etidronate, and is subsequently cleared from serum by 24 h. This highly specific complex of **fetuin**, MGP, and mineral prevents the growth, aggregation, and precipitation of the mineral component, which indicates that the previously reported calcification inhibitory activities of **fetuin** and MGP may be related to their ability to form stable complexes with nascent mineral nuclei. Treatment with the vitamin. . .

DETD . . . within 6 h, and that this elevation is caused by the unexpected appearance of a novel complex of calcium, phosphate, **fetuin**, and MGP in serum following etidronate injection. The structure and properties of this complex have direct relevance to an understanding. . .

DETD [0194] Biochemical Characterization of the Complex Between Calcium, Phosphate, **Fetuin**, and MGP.

DETD [0211] Centrifugational Evidence for a Complex of Calcium, Phosphate, **Fetuin**, and MGP in the Serum of Etidronate-Treated Rats.

DETD . . . subjected to N-terminal protein sequencing, one sequence was obtained, A-P-Q-G-A-G-L-G-F-R-(SEQ ID NO: _____), which matches the N-terminal sequence of rat **fetuin** (Ohnishi et al. (1993) J. Bone and Mineral Res. 8: 367-377). The other major band in the gel had an. . . total Coomassie staining; this band was identified as rat serum albumin by N-terminal sequence analysis. Based on the recovery of **fetuin** in the pellet, we estimate the weight ratio of **fetuin** to mineral phosphate in the pellet to be 3.4 mg/mg. Since the supernatant level of calcium and phosphate remained above. . .

DETD [0215] Gel Filtration Evidence for a High Molecular Weight Complex of Calcium, Phosphate, **Fetuin**, and MGP in the Serum of Etidronate-Treated Rats.

DETD . . . to PVDF. N-terminal protein sequencing of this 59 kDa band revealed that its sequence matched the N-terminal sequence of rat

fetuin (Ohnishi et al. (1993) J. Bone and Mineral Res. 8: 367-377). Comparison of the SDS-PAGE for fraction 23 from the. . .

DETD [0218] To estimate the amount of **fetuin** in the high molecular weight phosphate peak fractions, we performed two repeat SDS-PAGE analyses of fractions 22-24 of FIG. 12 upper together with lanes containing known amounts of pure **fetuin**. Quantitative analysis of the amount of coomassie staining in these **fetuin** bands using a densitometer yielded an estimate of 630 .mu.g **fetuin** in fractions 22-24. The phosphate content of these fractions is 83 .mu.g phosphate, and the weight ratio of **fetuin** to phosphate is 7.6 mg/mg. The total MGP content of fractions 22-24 is 11 .mu.g (FIG. 12), and the calculated molar ratio of MGP to **fetuin** in these fractions is 1: 8.

DETD . . . studies have shown that the doses of etidronate used here to cause the appearance of the complex of calcium, phosphate, **fetuin**, and MGP in serum also cause the inhibition of the normal calcification of bone and cartilage, resulting in the formation. . . in the proximal tibia. In the present studies we sought to determine whether the timing of the appearance of the calcium-phosphate-**fetuin**-MGP complex in serum correlates with the inhibition of growth plate cartilage mineralization. As seen in FIG. 6, microradiographs of the. . .

DETD . . . the .gamma.-carboxylation of MGP is necessary for the accumulation of the protein in the serum complex of calcium, phosphate, and **fetuin**, rats were injected with warfarin 2 h prior to the administration of etidronate in order to ensure that all MGP. . . electrophoresis of the high molecular weight phosphate-containing peak from the Sephacryl S300 chromatogram (data not shown) demonstrated the presence of **fetuin** at the level found in previous experiments (see FIG. 5), which indicates that the incorporation of **fetuin** into the serum mineral complex is independent of the presence of MGP.

DETD . . . etidronate dose, since the protein mineral complex found in serum the 8 mg/100 g dose does not sediment upon centrifugation. **Fetuin** is the major protein component of the serum mineral complex, with an estimated weight ratio of **fetuin** to mineral of 4.4 for the complex found in serum at the 8 mg/100 g etidronate dose, and an estimated ratio of **fetuin** to mineral of 1.9 at the 32 mg/100 g dose of etidronate. The MGP content of the serum mineral complex increases with time after etidronate injection, reaching a molar ratio of MGP to **fetuin** of 1:8. If the average molecular weight of the serum mineral complex were 550,000 daltons, the complex found in serum 6 h following treatment with the 8 mg/100 g dose of etidronate would consist of approximately 8 **fetuin** molecules, 1 MGP molecule, 790 atoms of calcium, and 580 molecules of phosphate. It should be noted that these calculations are based on the assumption that the only protein constituents of the complex are **fetuin** and MGP, and that the SDS gel shown in FIG. 3 indicates that higher molecular weight proteins could in fact. . .

DETD [0228] Role of **Fetuin** in the Serum Complex.

DETD [0229] The most abundant component of the serum complex is **fetuin**, not mineral or MGP, and it seems probable that the properties of the complex largely reflect the presence of **fetuin** in it. It is our hypothesis that **fetuin** molecules aggregate on the surface of the mineral nuclei and thereby prevent growth of the mineral phase and the generation of additional crystal nuclei. We believe that the most likely role for the protein component of **fetuin** is to mediate the binding of **fetuin** to mineral and to associate laterally with other **fetuin** molecules on the mineral surface to inhibit crystal growth. We further speculate that the 5 oligosaccharide moities of **fetuin**, which account for 25% of its weight, project away from the mineral and into the surrounding aqueous phase. The functions of oligosaccharides in **fetuin**

would be to lower the density of the mineral complex so that it will not sediment in serum and to. . .

DETD [0230] Previous studies have demonstrated that **fetuin** inhibits the sedimentation of calcium from supersaturated solutions of calcium and phosphate after centrifugation for 5 min at 15,000.times. g (Schinke et al. (1996) J. Biol. Chem. 271: 20789-20796). **Fetuin** in fact accounts for roughly half of the inhibitory activity found in serum. Although the mechanism by which **fetuin** inhibits calcium precipitation was not identified in these studies, the inhibitory activity was shown to be mediated by acidic amino acids clustered in the D1 cystatin-like domain of **fetuin**. Our present results are consistent with the putative calcification inhibitor activity of **fetuin** identified in these earlier studies, and suggest that this action of the protein could be associated with its ability to. . .

DETD [0231] **Fetuin** is known to be a major component of serum as well as a major constituent of the extracellular bone matrix (Kazi et al. (1998) J. Biochem. 124: 179-186; Triffitt et al. (1976) Nature 262: 226-227), and either **fetuin** pool could be the primary source of the **fetuin** found in the serum mineral complex. An important objective of future studies will be to determine the origin of **fetuin** in the serum mineral complex, and to evaluate the possibility that etidronate treatment could directly stimulate the synthesis of **fetuin** by liver or bone.

DETD . . . The alternative hypothesis for the 30 fold increase in serum MGP following etidronate administration is that the presence of the **fetuin** mineral complex in serum could stimulate a dramatic increase in the rate of MGP synthesis by tissues which contribute MGP. . .

DETD [0234] The present studies demonstrate that MGP binds to the **fetuin** mineral complex with considerable strength and specificity. The gel filtration analysis of the elution position of MGP antigen (FIG. 12. . . serum MGP in equilibrium with MGP bound to the complex must be very low. The binding of MGP to the **fetuin** mineral complex must also be highly specific, since we could detect no other Coomassie stained proteins associated with the complex other than **fetuin** and MGP (see FIG. 13). The specificity of this interaction is further supported by the observation that the structurally related. . .

DETD [0235] The ability of MGP to bind with great avidity to the mineral complex in spite of the presence of **fetuin** suggests that MGP could in fact have a greater affinity for mineral than **fetuin**, and so could be the stronger inhibitor of crystal growth. This possibility is supported by the observation that targeted deletion. . . and extensive calcification of the elastic lamellae of arteries beginning at birth (Luo et al. (1997) Nature 386: 78-81), while **fetuin** deficient mice have no evidence of soft tissue calcification except for the specialized case of occasional microcalcifications in a few. . . 272: 31496-31503). Without being bound to a particular theory, we believe the failure of soft tissues to calcify in the **fetuin** deficient mouse is due in part to the ability of MGP to inhibit calcification, and that the capacity of serum. . . on the ability to inhibit calcification in serum, such as is imposed by a high dose of etidronate, will cause **fetuin** deficient mice to experience a massive rate of mineral formation, a mineralization which cannot be retarded by the low capacity inhibitory function of serum MGP. A second prediction of this hypothesis is that warfarin treatment and the **fetuin** gene deletion should act synergistically to produce more rapid ectopic calcification than is found with either condition alone.

DETD [0236] While we have focused here on the ability of **fetuin** and MGP to prevent the growth of the mineral component of the serum complex,

it is important to note that both proteins have other important biological activities. **Fetuin** binds transforming growth factor-.beta. (TGF-.beta.) and bone morphogenic protein--2 (BMP-2) and blocks the osteogenic activity of these cytokines in cell. . . (Bostrom et al. (2001) J. Biol. Chem. 276(17), 14044-14052). An important goal of future studies will be to determine whether **fetuin** and MGP retain their ability to block the activity of cytokines when they are part of the serum complex.

CLM What is claimed is:

1. A method of determining the **risk** for calcification of arteries and other soft tissues in a mammal, said method comprising: detecting the level of a **fetuin**-mineral complex in blood from said mammal, wherein an increased level of **fetuin** mineral complex as compared to that found in a control indicates that said mammal is at increased **risk** for calcification of arteries and other soft tissues.

6. The method of claim 1, wherein said detecting comprises detecting the amount of **fetuin** comprising a sample of a **fetuin** mineral complex.

. . . method of claim 1, wherein said detecting comprises detecting the amount of matrix Gla protein comprising a sample of a **fetuin** mineral complex.

. . . method of claim 1, wherein said detecting comprises detecting the amount of secreted phosphoprotein 24 comprising a sample of a **fetuin** mineral complex.

. . . method of claim 1, wherein said detecting comprises detecting the amount of platelet factor 4 comprising a sample of a **fetuin** mineral complex.

. . . 10. The method of claim 1, wherein said detecting comprises detecting the amount of calcium comprising a sample of a **fetuin** mineral complex.

. . . 11. The method of claim 1, wherein said detecting comprises detecting the amount of phosphate comprising a sample of a **fetuin** mineral complex.

. . . method of claim 1, wherein said detecting comprises detecting the amount of a mineral phase comprising a sample of a **fetuin** mineral complex.

. . . arteries and other soft tissues, said method comprising: administering a test agent to a mammal; detecting the level of a **fetuin**-mineral complex in blood from said mammal, wherein a decreased level of **fetuin** mineral complex as compared to that found in a control indicates that said test agent reduces or amelioriates one or. . .

17. The method of claim 13, wherein said control is a predetermined concentration of a **fetuin**-mineral complex.

20. The method of claim 13, wherein said detecting comprises detecting the amount of **fetuin** comprising a sample of a **fetuin** mineral complex.

. . . method of claim 13, wherein said detecting comprises detecting the amount of matrix Gla protein comprising a sample of a **fetuin** mineral complex.

. . . of the calcification of arteries and other soft tissues in a mammal, said method comprising: detecting the level of a **fetuin** -mineral complex in blood from said mammal at one or more times during or after the course of said treatment, wherein a decreased level of **fetuin** mineral complex as compared to that found in a control indicates that said treatment reduces or amelioriates one or more. . .
25. The method of claim 22, wherein said control is a predetermined concentration of a **fetuin**-mineral complex.

26. The method of claim 22, wherein said detecting comprises detecting the amount of **fetuin** comprising a sample of a **fetuin** mineral complex.

. . . method of claim 22, wherein said detecting comprises detecting the amount of matrix Gla protein comprising a sample of a **fetuin** mineral complex.

. . . method of claim 22, wherein said detecting comprises detecting the amount of secreted phosphoprotein 24 comprising a sample of a **fetuin** mineral complex.

. . . method of claim 22, wherein said detecting comprises detecting the amount of platelet factor 4 comprising a sample of a **fetuin** mineral complex.

. . . 30. The method of claim 22 wherein said detecting comprises detecting the amount of calcium comprising a sample of a **fetuin** mineral complex.

. . . 31. The method of claim 22, wherein said detecting comprises detecting the amount of phosphate comprising a sample of a **fetuin** mineral complex.

. . . method of claim 22, wherein said detecting comprises detecting the amount of a mineral phase comprising a sample of a **fetuin** mineral complex.

33. A method of determining the **risk** for atherosclerosis in a mammal, said method comprising: detecting the level of a **fetuin** -mineral complex in blood from said mammal, wherein an increased level of **fetuin** mineral complex as compared to that found in a control indicates that said mammal is at increased **risk** for atherosclerosis.
37. The method of claim 33, wherein said detecting comprises detecting the amount of **fetuin** comprising a sample of a **fetuin** mineral complex.

. . . method of claim 33, wherein said detecting comprises detecting the amount of matrix Gla protein comprising a sample of a **fetuin** mineral complex.

. . . method of claim 33, wherein said detecting comprises detecting the amount of secreted phosphoprotein 24 comprising a sample of a **fetuin** mineral complex.

. . . method of claim 33, wherein said detecting comprises detecting the amount of platelet factor 4 comprising a sample of a **fetuin** mineral complex.

. . . 41. The method of claim 33, wherein said detecting comprises detecting the amount of calcium comprising a sample of a **fetuin** mineral complex.

. . . 42. The method of claim 33, wherein said detecting comprises detecting the amount of phosphate comprising a sample of a **fetuin** mineral complex.

. . . method of claim 33, wherein said detecting comprises detecting the amount of a mineral phase comprising a sample of a **fetuin** mineral complex.

. . . a treatment for one or more symptoms of atherosclerosis in a mammal, said method comprising: detecting the level of a **fetuin** -mineral complex in blood from said mammal at one or more times during or after the course of said treatment, wherein a decreased level of **fetuin** mineral complex as compared to that found in a control indicates that said treatment reduces or amelioriates one or more. . . 47. The method of claim 44, wherein said control is a predetermined concentration of a **fetuin**-mineral complex.

48. The method of claim 44, wherein said detecting comprises detecting the amount of **fetuin** comprising a sample of a **fetuin** mineral complex.

. . . method of claim 44, wherein said detecting comprises detecting the amount of matrix Gla protein comprising a sample of a **fetuin** mineral complex.

. . . method of claim 44, wherein said detecting comprises detecting the amount of secreted phosphoprotein 24 comprising a sample of a **fetuin** mineral complex.

. . . method of claim 44, wherein said detecting comprises detecting the amount of platelet factor 4 comprising a sample of a **fetuin** mineral complex.

. . . 52. The method of claim 44, wherein said detecting comprises detecting the amount of calcium comprising a sample of a **fetuin** mineral complex.

. . . 53. The method of claim 44, wherein said detecting comprises detecting the amount of phosphate comprising a sample of a **fetuin** mineral complex.

. . . method of claim 44, wherein said detecting comprises detecting the amount of a mineral phase comprising a sample of a **fetuin** mineral complex.

55. A method of determining the **risk** for osteoporosis in a mammal, said method comprising: detecting the level of a **fetuin** -mineral complex in blood from said mammal, wherein an increased level of **fetuin** mineral complex as compared to that found in a control indicates that said mammal is at increased **risk** for osteoporosis.
59. The method of claim 55, wherein said detecting comprises detecting the amount of **fetuin** comprising a sample of a **fetuin** mineral complex.

. . . method of claim 55, wherein said detecting comprises detecting the amount of matrix Gla protein comprising a sample of a **fetuin** mineral complex.

. . . method of claim 55, wherein said detecting comprises detecting the amount of secreted phosphoprotein 24 comprising a sample of a

fetuin mineral complex. The method of claim 55, wherein said detecting comprises detecting the amount of platelet factor 4 comprising a sample of a **fetuin** mineral complex.

. . . 62. The method of claim 55, wherein said detecting comprises detecting the amount of calcium comprising a sample of a **fetuin** mineral complex.

. . . 63. The method of claim 55, wherein said detecting comprises detecting the amount of phosphate comprising a sample of a **fetuin** mineral complex.

. . . method of claim 55, wherein said detecting comprises detecting the amount of a mineral phase comprising a sample of a **fetuin** mineral complex.

. . . 65. A method of monitoring the efficacy of a treatment of osteoporosis, said method comprising: detecting the level of a **fetuin**-mineral complex in blood from said mammal at one or more times during or after the course of said treatment, wherein a decreased level of **fetuin** mineral complex as compared to that found in a control indicates that said treatment reduces or amelioriates one or more. . .

68. The method of claim 65, wherein said control is a predetermined concentration of a **fetuin**-mineral complex.

69. The method of claim 65, wherein said detecting comprises detecting the amount of **fetuin** comprising a sample of a **fetuin** mineral complex.

. . . method of claim 65, wherein said detecting comprises detecting the amount of matrix Gla protein comprising a sample of a **fetuin** mineral complex.

. . . method of claim 65, wherein said detecting comprises detecting the amount of secreted phosphoprotein 24 comprising a sample of a **fetuin** mineral complex.

. . . method of claim 65, wherein said detecting comprises detecting the amount of platelet factor 4 comprising a sample of a **fetuin** mineral complex.

. . . 73. The method of claim 65, wherein said detecting comprises detecting the amount of calcium comprising a sample of a **fetuin** mineral complex.

. . . 74. The method of claim 65, wherein said detecting comprises detecting the amount of phosphate comprising a sample of a **fetuin** mineral complex.

. . . method of claim 65, wherein said detecting comprises detecting the amount of a mineral phase comprising a sample of a **fetuin** mineral complex.

L2 ANSWER 6 OF 9 USPATFULL on STN
AN 2003:10656 USPATFULL
TI Novel FGF homologs
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PI US 2003008351 A1 20030109
AI US 2002-81347 A1 20020221 (10)
RLI Continuation of Ser. No. US 1999-229947, filed on 13 Jan 1999, PENDING
PRAI US 1996-28646P 19961016 (60)
DT Utility
FS APPLICATION
LREP Deborah A. Sawislak, Patent Department, ZymoGenetics, Inc., 1201 Eastlake Avenue East, Seattle, WA, 98102
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 3583
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to polynucleotide and polypeptide molecules for ZFGF5 a novel member of the FGF family. The polypeptides, and polynucleotides encoding them, are proliferative for muscle cells, in particular cardiac cells and may be used for remodeling cardiac tissue and improving cardiac function. The present invention also includes antibodies to the zFGF5 polypeptides.
SUMM . . . accounts for 750,000 hospital admissions per year in the U.S., with more than 5 million people diagnosed with coronary disease. **Risk** factors for MI include diabetes mellitus, hypertension, truncal obesity, smoking, high levels of low density lipoprotein in the plasma or. . .
DETD [0167] 10 .mu.g/ml **fetuin** (Aldrich, Milwaukee, Wis.)
DETD . . . circulation. High levels of expression and physiological effects have been demonstrated (Ohwada et al., Blood 88:768-774, 1996; Stevenson et al., **Arteriosclerosis**, Thrombosis and Vascular Biology, 15:479-484, 1995; Setoguchi et al., Blood 84:2946-2953, 1994; and Sakamoto et al., Proc. Natl. Acad. Sci.. . .
DETD . . . using Lipofectamine.TM. (Gibco BRL), in serum free (SF) media formulation (Ham's F12, 10 mg/ml transferrin, 5 mg/ml insulin, 2 mg/ml **fetuin**, 1% L-glutamine and 1% sodium pyruvate). ZFGF5/pZMP6 is diluted into 15 ml tubes to a total final volume of 640. . .

L2 ANSWER 7 OF 9 USPATFULL on STN
AN 2002:45596 USPATFULL
TI FGF Homologs
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PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 6352971 B1 20020305
AI US 1999-368951 19990805 (9)
RLI Division of Ser. No. US 1997-951822, filed on 16 Oct 1997, now patented, Pat. No. US 5989866
PRAI US 1996-28646P 19961016 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Mertz, Prema; Assistant Examiner: Murphy, Joseph F.
LREP Sawislak, Deborah A.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 2656

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to polynucleotide and polypeptide molecules for zFGF-5 a novel member of the FGF family. The polypeptides, and polynucleotides encoding them, are proliferative for muscle cells and may be used for remodelling cardiac tissue and improving cardiac function. The present invention also includes antibodies to the zFGF-5 polypeptides.
SUMM . . . accounts for 750,000 hospital admissions per year in the U.S., with more than 5 million people diagnosed with coronary disease. **Risk** factors for MI include diabetes mellitus, hypertension, truncal obesity, smoking, high levels of low density lipoprotein in the plasma or. . .
DETD . . . St. Louis, MO)
1 mM sodium pyruvate (Sigma, St. Louis, MO)
25 mM Hepes (Sigma, St. Louis, MO)
10 .mu.g/ml **fetuin** (Aldrich, Milwaukee, WI)
50 .mu.g/ml insulin (Gibco-BRL)
3 ng/ml selenium (Aldrich, Milwaukee, WI)
20 .mu.g/ml transferrin (JRH, Lenexa, KS)
DETD . . . circulation. High levels of expression and physiological effects have been demonstrated (Ohwada et al., Blood 88:768-774, 1996; Stevenson et al., **Arteriosclerosis**, Thrombosis and Vascular Biology, 15:479-484, 1995; Setoguchi et al., Blood 84:2946-2953, 1994; and Sakamoto et al., Proc. Natl. Acad. Sci.. . .

L2 ANSWER 8 OF 9 USPATFULL on STN
AN 2000:43944 USPATFULL
TI Purified and recombinant antigenic protein associated with abdominal aortic aneurysm (AAA) disease, and diagnostic and therapeutic use thereof
IN Tilson, Martin David, Scarsdale, NY, United States
PA The Trustees of Columbia University, New York, NY, United States (U.S. corporation)
PI US 6048704 20000411
AI US 1997-812586 19970307 (8)
PRAI US 1996-12976P 19960307 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Housel, James C.; Assistant Examiner: Swartz, Rodney P.
LREP White, John P.Cooper & Dunham LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 22 Drawing Figure(s); 24 Drawing Page(s)
LN.CNT 3522
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides an isolated protein of approximately 40 kDa which is purified from human aortic tissue and immunoreactive with AAA-associated immunoglobulin. Also provided are a method of diagnosing AAA disease in a subject using said isolated protein and a pharmaceutical composition comprising said isolated protein. A method of alleviating AAA disease in a subject comprising administering said pharmaceutical composition comprising the isolated protein is also provided. The subject invention also provides a recombinantly produced human aortic protein which is immunoreactive with AAA-associated immunoglobulin. Also provided are a method of diagnosing AAA disease in a subject using said recombinantly produced protein and a pharmaceutical composition comprising said recombinantly produced protein. A method of alleviating AAA disease in a subject comprising administering said pharmaceutical composition comprising the recombinantly produced protein is also provided.
DRWD . . . Control glycoprotein transferrin (TRNSF) reacted with SNA,

indicating sialic acid terminally linked alpha (2-6) to galactose or N-acetylgalactosamine. Control glycoprotein **fetuin** (FETN) reacted with SNA, MAA (indicating sialic acid terminally linked alpha (2-3) to galactose), and DSA (indicating galactose beta (1-4). . .

DETD 7. DePalma R G, Sidaway A N, Giordana J M. Associated aetiological and atherosclerotic **risk** factors in abdominal aneurysms. in: The Cause and Management of Aneurysms, ed. R M Greenhalgh, J A Mannick, J T. . .

DETD . . . H, Nagase H, Tilson M D. Identification of matrix metalloproteinases 3 (stromelysin-1) and 9 (gelatinase B) in abdominal aortic aneurysm. **Arteriosclerosis** and Thrombosis, 1994; 14: 1315-1320.

L2 ANSWER 9 OF 9 USPATFULL on STN
AN 1999:150969 USPATFULL
TI FGF homologs
IN Deisher, Theresa A., Seattle, WA, United States
Conklin, Darrell C., Seattle, WA, United States
Raymond, Fenella, Seattle, WA, United States
Bukowski, Thomas R., Seattle, WA, United States
Holderman, Susan D., Kirkland, WA, United States
Hansen, Birgit, Seattle, WA, United States
Sheppard, Paul O., Redmond, WA, United States
PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 5989866 19991123
AI US 1997-951822 19971016 (8)
PRAI US 1996-28646P 19961016 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John; Assistant Examiner: Saoud, Christine
LREP Sawislak, Deborah A.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 2660
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to polynucleotide and polypeptide molecules for zFGF-5 a novel member of the FGF family. The polypeptides, and polynucleotides encoding them, are proliferative for muscle cells and may be used for remodelling cardiac tissue and improving cardiac function. The present invention also includes antibodies to the zFGF-5 polypeptides.

SUMM . . . accounts for 750,000 hospital admissions per year in the U.S., with more than 5 million people diagnosed with coronary disease. **Risk** factors for MI include diabetes mellitus, hypertension, truncal obesity, smoking, high levels of low density lipoprotein in the plasma or. . .

DETD . . . mg/ml L-glutamine (Sigma, St. Louis, MO)
1 mM sodium pyruvate (Sigma, St. Louis, MO)
25 mM Hepes (Sigma, St. Louis, MO)
10 .mu.g/ml **fetuin** (Aldrich, Milwaukee, WI)
50 .mu.g/ml insulin (Gibco-BRL)
3 ng/ml selenium (Aldrich, Milwaukee, WI)
20 .mu.g/ml transferrin (JRH, Lenexa, KS)

DETD . . . circulation. High levels of expression and physiological effects have been demonstrated (Ohwada et al., Blood 88:768-774, 1996; Stevenson et al., **Arteriosclerosis**, Thrombosis and Vascular Biology, 15:479-484, 1995; Setoguchi et al., Blood 84:2946-2953, 1994; and Sakamoto et al., Proc. Natl. Acad. Sci.. . .